

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

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

February 15-16, 2012

The National Advisory Environmental Health Sciences Council convened its one hundred thirty-fifth regular meeting on February 15, 2012 in the Rall Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Dr. Linda Birnbaum presided as Chair.

The meeting was open to the public on February 15, 2012 from 8:30 a.m. to 1:45 p.m. and on February 16, 2012 from 8:30 a.m. to 12:18 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 February 15, 2012 from 2:15 p.m. to 5:00 p.m. for consideration of grant applications. Notice of the meeting was published in the *Federal Register*.

Council Members Present

Stephen Baylin, MD
Kim Boekelheide, MD, PhD
Julia Brody, PhD
Marie-Francoise Chesselet, MD, PhD
Lisa Conti, DVM, MPH
Steve Dearwent, PhD
Richard Finnell, PhD
Thomas Gasiewicz, PhD
Andrea Hricko, MPH
Howard Hu, MD, MPH, ScD
Randall Kramer, PhD (February 16, 2012)
Mary M. Lee, MD
Grace LeMasters, PhD
R. Stephen Lloyd, PhD
Yvonne Maddox, PhD
Thomas McKone, PhD (February 16, 2012, by phone)
Sem Phan, MD, PhD
Edward Postlethwait, PhD
Palmer Taylor, PhD
Viola Waghiyi

Deborah Winn, PhD
Nsedu Obot Witherspoon, MPH
Elizabeth Yeampierre, JD

NIEHS Staff

Kathy Ahlmark
Janice Allen, PhD
Bruce Androphy, JD
Robin Arnette, PhD
Joellen Austin
Beth Anderson
Clifton Baldwin
David Balshaw, PhD
Martha Barnes
Linda Bass, PhD
Sharon Beard
Linda Birnbaum, PhD
John Bucher, PhD
Danielle Carlin
Trisha Castranio
Lisa Chadwick, PhD
Pamela Clark
Jennifer Collins
Gwen Collman, PhD
Helena Davis
Caroline Dilworth, PhD
Christina Drew, PhD
Dorothy Duke
Sally Eckert-Tilotta, PhD
Lisa Edwards
Yolanda Eskridge-Nyass
Symma Finn, PhD
Christine Flowers
Mary Gant
Antonio Gatling
Barbara Gittleman
Kimberly Gray, PhD
Astrid Haugen
Jerry Heindel, PhD
Heather Henry, PhD
Michael Humble, PhD
Barbara Johnson
Laurie Johnson
Paul Jung, MD, MPH
Annette Kirshner, PhD

Cindy Lawler, PhD
Chris Long
Robin Mackar
J. Patrick Mastin, PhD
Kim McAllister, PhD
Rose Anne McGee
Liz McNair
Fred Miller, MD, PhD
Sri Nadadur, PhD
Teresa Nesbitt, DVM, PhD
Sheila Newton, PhD
Liam O'Fallon
Ted Outwater
Anshul Pandya, PhD
Jerry Phelps
Kristi Pettibone
Edward Pope
Molly Puente
Scott Redman
Leslie Reinlib, PhD
Andrew Rooney, PhD
Thad Schug, PhD
Maria Shatz, PhD
Daniel Shaughnessy, PhD
Carol Shreffler, PhD
William A. Suk, PhD, MPH
Kimberly Thigpen Tart, JD
Claudia Thompson, PhD
Frederick Tyson, PhD
James Williams
Richard Woychik, PhD
Darryl Zeldin, MD

Members of the Public Present

Robert Croyle, PhD, NCI
Philippe Grandjean, DMSc, MD, Harvard School of Public Health
Ernie Hood, Scribe
Nancy Lamontagne, MDB Inc.
Tim McAdams, Westat
Branka Sekis, SSS
David Shore, Westat

I. Call To Order and Opening Remarks

Dr. Linda Birnbaum, Director of NIEHS and NTP, welcomed attendees and called the meeting to order. She mentioned that Council members Dr. Tom McKone, Dr. Chris Bradfield, and Dr. Jerald Schnoor were absent from the meeting. She welcomed new Council members Dr. Kim Boekelheide, Dr. Lisa Conti, Dr. Howard Hu, Dr. Edward Postlethwait, and Viola Waghiyi. She noted that this would be the last meeting for retiring Council members Dr. Stephen Baylin and Dr. Christopher Bradfield. She then asked all present in the room to introduce themselves, which they did.

II. Review of Confidentiality and Conflict of Interest

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

III. Consideration of September 2011 Meeting Minutes

Approval of the September 2011 minutes was moved (Dr. Lloyd) and seconded (Dr. Lee), and Council voted unanimously to approve the minutes. Dr. Collman mentioned that the new members of Council would not vote in this meeting. She also noted the dates of the upcoming Council meetings for members to put on their calendars.

IV. Report of the Director, NIEHS

Dr. Birnbaum briefly updated Council on the status of the NIEHS Strategic Planning process. She shared the “pillars” or “clouds” graphic depiction of the overlapping elements of the NIEHS mission, and the most recent versions of the Draft Mission Statement and Draft Vision Statement.

She shared recent staff changes. Dr. Darryl Zeldin took over as Scientific Director in October. The search for a new Clinical Director is advancing. Also, Dr. William Copeland has been named Chief of the Laboratory of Molecular Genetics. She also noted the recent death of former NTP toxicologist Dr. Kamal Abdo.

She reported on three current initiatives, one at NIH and two at NIEHS. The first is an effort by NIH to make its branding more consistent and recognizable by working to create a single logo, and developing a new slogan: “NIH—Turning Discovery Into Health.” Also, she announced that *Environmental Health Perspectives* (EHP) will be going paperless by January 2013, and described progress with an initiative designed to improve the NIEHS organizational climate called the NIEHS Pulse Survey and Action Plan. It includes action in communication, career development and training, and staff recognition and promotion. Development of a new Intranet site will be perhaps the most visible element.

Turning to the NIEHS budget outlook, Dr. Birnbaum reported that NIH did “relatively well” in FY2012, given the state of the economy. Although overall NIH funding fell slightly compared to the FY2011 Continuing Resolution, NIEHS funding actually saw a slight increase, although that amount was slightly less than FY2010. In the President’s FY2013 budget request, NIH funding is basically flat, and NIEHS funding is very slightly lower. Superfund funding has been steady and is expected to remain at current levels. The annual \$10 million NIEHS/Department of Energy training funding is expected to continue. It is clear, she said, that a budget will not be passed at least until after the election in November. There is also the possibility of a 10% cut in funding due to budget sequestration, and NIEHS and NIH are working to project how that requirement might be accommodated if it comes to pass.

Reporting on legislative activities, she noted that the National Center for Advancing Translational Sciences (NCATS) was established in December, with a budget of more than \$576 million, while the National Center for Research Resources was eliminated. The National Children’s Study continues with roughly the same budget, but faces an approximately \$50-60 million cut, partly from adoption of a much less expensive recruitment strategy. The NIH Common Fund continues to grow. She reported that there has been little activity recently in terms of Congressional testimony by her or Dr. Collins.

She shared recent scientific advances from NIEHS-conducted or supported research. First, she summarized a study by intramural investigator Serena Dudek that showed that a region of the hippocampus called CA2 contains caffeine receptors and is involved in synaptic plasticity, with exposure to caffeine causing long-term plasticity changes. A publication associated with the Sister Study shed light on risk factors for uterine fibroids, particularly among African-American women. A study that emerged from the NTP Laboratory addressed the interaction between UV light and arsenic to induce skin cancer. An NIEHS-funded study using the Norwegian Mother and Child Cohort showed that maternal use of folic acid supplements during the period from 4 weeks before to 8 weeks after conception was associated with a reduced risk of severe language delay among offspring. A study by Dr. Philippe Grandjean and colleagues from the Harvard School of Public Health in their Faroe Islands birth cohort found an association of elevated perfluorinated compounds (PFC) exposure with reduced antibody immune response to childhood vaccinations. A study that emerged from an NIEHS-funded Children’s Center in California reported that parental stress increases the detrimental effect of traffic exposure on children’s lung function compared to children who grow up in households with low psychosocial stress.

Turning to other institute news and highlights, Dr. Birnbaum recounted several important recent activities related to autism and neurotoxicology. NIEHS and EHP were among the sponsors of the 27th International Neurotoxicology Conference held in October 2011

in RTP, which focused on Environmentally Triggered Neurodevelopmental Disorders. November saw a meeting called *Bioinformatics and Computational Approaches to Integrate Genes and Environment in Autism Research*, organized by Dr. Cindy Lawler. In December, NIEHS partnered with four other NIH ICs to launch a data sharing collaboration between the National Database for Autism Research and the Autism Genetic Resource Exchange, constituting the largest repository to date of genetic, phenotypic, clinical and medical imaging data related to autism research. In January, NIEHS participated in the Environmental Influences on Neurodevelopment workshop held at UCLA.

Several meetings highlighted NIEHS leadership in public health, including the joint meeting in October with PAHO/WHO collaborating center grantees in sustainable development and environmental health, which brought PAHO/WHO grantees from around the world to RTP and provided a unique opportunity for NIEHS staffers to interact with far-flung colleagues. In November, Dr. Birnbaum held an NIEHS Community Forum in Los Angeles focused on the issue of traffic pollution. Also, the National Academy of Sciences recently released a report funded in part by NIEHS called *Improving Health in the United States: The Role of Health Impact Assessment*.

Among other important meetings and conferences, Dr. Mike Humble organized a Toxicology and Infectious Disease workshop in October, a look at two areas that will collide more and more with globalization and climate change. Researchers from the NIEHS nanotechnology Grand Opportunities program met in December to share their findings at the final meeting of the program, which began in 2009 with ARRA funding. Also, NIEHS and Superfund staff participated in the mHealth summit, a conference focused on the role of mobile technologies in health. The NIEHS-sponsored Standing Committee on the Use of Emerging Science for Environmental Health Decisions of the National Academy of Sciences held a workshop in December on *Emerging Technologies for Measuring Individual Exposomes*. A first-of-its-kind meeting was held at NIEHS to discuss the issues surrounding exposure to erionite, an asbestos-like material that has been linked to malignant mesothelioma. It was organized by Senior Medical Advisor Dr. Aubrey Miller. In February, NIEHS staff held a workshop to explore the critically important issue of data sharing among different environmental health disciplines and researchers.

Upcoming meetings include the 5th Annual NIH Conference on the Science of Dissemination and Implementation: Research at the Crossroads, to be held March 19-20, 2012. There will be a Children's Environmental Health & Disease Prevention Research Meeting at NIH on March 6. The Partners in Environmental Public Health will hold their 2012 meet at NIH March 7-8. The NAS Emerging Science for Environmental Health Decisions will hold a meeting April 18-19 at the Academy on *Individual*

Variability. Early in May, the NIEHS-sponsored Institute of Medicine Round Table will hold a workshop on the issue of hydro-fracking.

Recent awards received by NIEHS and NTP staff members include an NIH Director's Award given in 2011 to the NIEHS Gulf oil spill response team. Also, Martha Barnes from the extramural program was included in a Director's Award for the Patient-Reported Outcomes Measurement Information System (PROMIS) Working Group. NIH also recognized 21 NIEHS fellows with FARE awards – Fellows Award for Research Excellence. That represented nearly 10% of the awards given among the 21 NIH ICs.

Four NIEHS scientists were honored at the recent NIEHS Science Day ceremonies. Dr. Lutz Birnbaumer was named Scientist of the Year; Dr. Scott Williams received the Early Career Award; Dr. Geoffrey Mueller was chosen as Outstanding Staff Scientists, and Dr. Donna Baird was named Mentor of the Year.

In other awards and recognitions reported by Dr. Birnbaum, Dr. David Eastmond, who chairs the NTP Board of Scientific Counselors, has been named a Ramazzini Fellow. NIEHS grantee Dr. David Eaton from the University of Washington was elected to the Institute of Medicine. Dr. Monica Ramiriz-Andreotta, a doctoral student at the University of Arizona, received the Karen Wetterhahn Memorial Award. Chip Hughes from the NIEHS Worker Training and Education Program was honored with the National Council for Occupational Safety and Health Tony Mazzocchi Award. Dr. Paul Foster of NTP has been inducted as a Fellow of the Academy of Toxicological Sciences. Former NIEHS/NTP Director Dr. Kenneth Olden has received the Richard and Barbara Hansen Leadership Award from the University of Iowa School of Public Health. Melissa Kerr, a student at North Carolina Central University and an intern for the NIEHS *Environmental Factor* newsletter won an award from the American Chemical Society for her work with the newsletter. Two grantees were honored by the Environmental Mutagen Society (EMS): Dr. Arthur Grollman from the State University of New York Stonybrook received the EMS Award, and Dr. Karen Huen from the University of California at Berkeley was recognized for the 2011 EMS top publication by a new investigator. Former grantee Dr. Louis Guillette received the Heinz Award for his pioneering research on the impact of toxic chemicals on wildlife and human health. Dr. Birnbaum congratulated staff and grantees for their achievements and recognition.

Ms. Witherspoon said she was pleased to hear that NIEHS would be participating in the discussion on hydro-fracking. She expressed concern about the difficulty of acquiring data on the Gulf oil spill. Dr. Birnbaum mentioned that NTP had organized a mini-symposium on hydro-fracking two months ago. She added that in the GuLF study, more than 10,000 clean-up workers have been recruited so far, with more than 2,000 in-

home interviews conducted. The research consortium comprised of 8 NIH ICs and led by NIEHS is examining other issues related to the spill, with four universities and 120 community groups participating in the research. She noted that the NTP research program and the Worker Education and Training program related to the Gulf oil spill are also continuing.

Dr. Hu inquired about the budget cut of at least \$50 million to the National Children's Study (NCS). He asked whether that would result in a reduction of the sample size. Dr. Birnbaum said that the sample size would remain at 100,000. She explained that the experience of the NCS vanguard centers had led to greatly improved recruiting methods that would improve efficiency and reduce costs. The study will adopt provider-based recruiting. Another change in methodology will be the abandonment of location-based recruiting – subjects will now continue to be followed regardless of where they live.

V. Strategic Plan Process

NIEHS Deputy Director Dr. Richard Woychik updated Council on the status of the institute's Strategic Planning Process, which he leads. He acknowledged the leadership provided by Dr. Birnbaum, the leadership group consisting of Dr. John Bucher, Dr. Fred Miller, Dr. Darryl Zeldin, Ms. Joellen Austin, and Dr. Sheila Newton, who wrote much of the existing draft material. For the benefit of the new Council members, he recapped the overall process, which will culminate in a new strategic plan for the institute to help determine its direction for the next five years. He said he would concentrate on the progress made in the process since the last Council meeting in September, 2011.

He recapped the Stakeholder Community Workshop, which was held in Research Triangle Park July 12-14. Approximately 170 participants attended, and ultimately 8 "overarching themes" were developed:

- Basic Research on Human Health and Disease
- Exposure Science and the Exposome
- Translational Science: Linking Biological Pathways and Bridging the Gaps to Activities that Move toward Actual Health Outcomes
- Collaborative and Integrative Approaches for Conducting Research
- Data Management and Analysis
- Environmental Health Disparities, Environmental Justice, and Climate Change
- Training of the Environmental Health Science Workforce
- Communication and Outreach

The next major step in the process was the Strategic Planning Workshop held in October, 2011 at Research Triangle Park, which included approximately 60 NIEHS and external participants. Day One was devoted to drafting mission and vision statements,

a “tag line, and supporting pillars. Day Two was devoted to elaborating upon and clarifying the supporting pillars.

The draft Mission Statement is:

The mission of the National Institute of Environmental Health Sciences is to discover how the environment affects people in order to promote healthier lives.

The draft Vision Statement reads:

The vision of the National Institute of Environmental Health Sciences is to provide global leadership for innovative research that improves public health by preventing disability and disease from our environment.

Dr. Woychik presented the graphic treatment of the diagram depicting the fundamental, interacting pillars upon which the mission and vision statements rest. The pillars are:

- Fundamental Research
- Exposure Research
- Translational Research
- Global Environmental Health and Health Disparities
- Training
- Communication/Outreach

Those pillars are surrounded by the overarching pillars of Integrative and Collaborative Approaches and Data Management. The pillars concept has also been characterized as “clouds.”

The next step in the process was for NIEHS leadership to work together to develop strategic goals based upon the pillars. After much consideration, 11 institutional goals were developed. The draft NIEHS Strategic Plan goals are:

1. Identify and understand fundamental shared mechanisms or common biological pathways (e.g., inflammation, epigenetic changes, oxidative stress, mutagenesis) underlying a broad range of complex diseases, in order to enable the development of broadly applicable prevention and intervention strategies.
 - a. Investigate the effects of the environment on genome structure and function.
 - b. Investigate the effects of the environment on the epigenetic regulation of biological and pathological processes.
 - c. Understand the role of key protective mechanisms and their regulation in determining resistance and susceptibility to environmental stressors.
 - d. Understand the normal processes of human development and identify environmental factors that contribute to altered function.

e. Develop a pipeline to integrate high throughput screening, cell systems and model organisms to identify fundamental mechanisms underlying responses to existing and emerging environmental toxicants and to better predict their relationship to disease.

2. Understand individual susceptibility across the life span to chronic, complex diseases resulting from environmental factors, in basic and population-based studies, to facilitate prevention and decrease public health burden.

- a. Using a life span approach, identify critical windows of susceptibility to the effects of environmental exposures.
- b. Deepen our understanding of dose response relationships to environmental factors across the lifespan.
- c. Study the factors that determine individual susceptibility to environmental stressors across the lifespan.

3. Transform exposure science by enabling consideration of the totality of human exposures and links to biological pathways and create a blueprint for incorporating exposure science into human health studies.

- a. Advance characterization of environmental exposures through improved exposure assessment at both the individual and population levels.
- b. Define and disseminate the concept of the exposome.
- c. Create tools and technologies, and the research capacity, needed to characterize the exposome.

4. Understand how combined environmental exposures affect disease pathogenesis.

- a. Assess the joint action of multiple environmental insults (including chemicals, non-chemical stressors, and nutritional components) on toxicity/disease and identify interactions resulting from combined exposures.
- b. Study the role of the human microbiome and its influence on environmental health; explore the role of the microbiome in responses to environmental exposures.
- c. Study the interactions of infectious agents with environmental exposures.
- d. Understand how non-chemical stressors (including socioeconomic, behavioral factors, etc.) interact with other

environmental exposures to impact human health outcomes, and identify preventive measures that could be taken.

5. Identify and respond to emerging environmental threats to human health on both a local and global scale.

- a. Enlist the capacity of the EHS research enterprise to elucidate information necessary for timely and effective public health action.
- b. Act proactively with other public health partners to provide appropriate responses to emerging environmental threats.
- c. Focus on research needs to help inform policy responses in public health situations in which lack of knowledge hampers policymaking (e.g., health effects of exposures related to hydrofracking or climate change, or exposures to engineered nanomaterials).

6. Establish an environmental health disparities research agenda to understand the disproportionate risks of disease and to define and support public health and prevention solutions in affected populations.

- a. Conduct community-based participatory research.
- b. Include research and education on the ethical, legal, and social implications of EHS research, including human participation issues, research integrity, reporting of results, and other issues.
- c. Develop and recommend or implement interventions to reduce or eliminate environmental exposures that cause the greatest burden of disease to affected populations.

7. Use knowledge management techniques to create a collaborative environment for the EHS community to encourage an interdisciplinary approach to investigate, analyze, and disseminate findings.

- a. Develop bioinformatics, biostatistics, and data integration tools to conduct interdisciplinary research for application to environmental health science.
- b. Develop and invest in publicly available resources and computational tools for integrating and analyzing environmental health data.

8. Enhance the teaching of EHS at all levels of education and training (K-professional) to increase scientific literacy and generate awareness of the health consequences of environmental exposures.

- a. Empower individuals at all levels of education with knowledge to make better health decisions.
- b. Use leadership and partnerships to strengthen EHS education and literacy, using research on effective EHS education strategies and creating mechanisms for educators to promote EHS education.
- c. Develop critical training programs in EHS research tailored for multiple groups (students, postdocs, foreign scientists, and science teachers).
- d. Incorporate EHS into Medical Education/Practice (nursing, MD, etc.) to increase awareness of environmental medicine in healthcare practice.

9. Inspire a diverse and well-trained cadre of scientists to move our transformative environmental health science forward; train the next generation of EHS leaders from a wider range of scientific disciplines and diverse backgrounds.

- a. Foster cross-disciplinary training in areas that are necessary but underrepresented in EHS (informatics, engineering, biobehavioral, etc.)
- b. Recruit trainees from other disciplines to diversify our science base.
- c. Ensure effective opportunities across the entire career trajectory, for young investigators' transition to independence and also for retraining of mid-career scientists and other EHS professionals.
- d. Promote the integration of EHS into Medical Education to increase the number of physician or nurse researchers that are trained in EHS.
- e. Build environmental health research capacity in those countries around the world experiencing the greatest burden of death, disease, and disability related to the environment.
- f. Increase diversity within training programs for environmental health scientists.

10. Evaluate the economic impact of policies, practices, and behaviors that reduce exposure to environmental toxicants through prevention of disease and disabilities; invest in research programs to test how prevention improves public health and minimizes economic burden.

- a. Develop an interdisciplinary research and training program in environmental health economics, to better understand the economic costs and benefits of environmental exposures, related diseases, and interventions to prevent exposures and diseases.

- b. Measure economic benefits and comparative effectiveness of NIEHS investments, employing health economics as a part of the NIEHS research agenda – developing the tools and databases to advance this research.
- c. Assist policymakers with systematic review and state-of-the-science assessments to help them make clinical/policy recommendations.

11. Promote bidirectional communication and collaboration between researchers and stakeholders (policy makers, clinicians, intervention/prevention practitioners, and the public) in order to advance research translation in the environmental health sciences.

- a. Promote NIEHS as a trusted and accessible source of EHS-based information. Increase NIEHS's reach and effectiveness in communication and outreach.
- b. Identify and expand our relevant stakeholder communities; enhance engagement to understand their priorities, concerns and needs related to EHS.
- c. Build and lead long-term federal and non-federal partnerships with health education agencies and mission-related stakeholder groups to create a pipeline for the coordination of disseminating scientific results to the public and also to hear back from their constituents.
- d. Conduct research as needed on effective EHS communication strategies (including risk communication).
- e. Develop an integrated, searchable knowledge base on the impact of environment on health.

Dr. Woychik concluded his presentation with a summary of the next steps in the process, leading to completion and implementation of the strategic plan. Public comment on all materials posted on the web is open through the end of February. The narrative around mission, vision, pillars and goals will be developed through the end of March. A draft of the final plan will be posted for public comment through the month of April. A final draft of the plan will be submitted for Council approval in May. Then implementation strategies will be developed by division directors working within their divisions to determine what will be done, when it will be done, and how much it will cost. Institute leadership will then integrate those strategies into an operational and financial plan for NIEHS for the next 5 years.

Initiating Council discussion, Dr. Woychik invited Dr. Bucher, Dr. Miller, Dr. Newton, Dr. Zeldin, and Ms. Austin to convene at the front of the room to entertain questions.

Ms. Yeampierre asked about Strategic Goal #4, in the context of whether long-term socioeconomic factors—even over generations—that would make certain populations particularly susceptible to disease, would be considered. Dr. Newton said that she had a good point. Dr. Woychik said that the concept had been very much a part of the consciousness, as all of the exposures must be evaluated, not just the immediate ones. Dr. Birnbaum cited the example of the Long Island Breast Cancer Study and PCBs as showing that exposures must be evaluated over long periods of time, as diseases such as cancer may take a very long time to develop after exposures. She noted the institute's major emphasis on early life exposures and their long-term impacts, including epigenetics, with the inclusion of parents' and even grandparents' exposures as well.

Dr. Maddox discussed the phenomenon of migration, when an individual or community is exposed in one area and then moves to another location. She said often it is not the environmental exposure involving toxins, but the influence of social and economic variations as well. She said she interpreted the point of Strategic Goal #4 in that context. Dr. Woychik pointed out that he had emphasized the words “non-chemical stressors” under that goal in his presentation, and that socioeconomic and behavioral factors were included in the goal's text as well. Dr. Birnbaum noted that there are already NIEHS grantees looking at those factors, but to go farther would require partnering with other NIH ICs as well as other organizations. She cited the example of partnerships with the Office of Behavioral and Social Science Research in the NIH Director's Office, with the hope that there will be more opportunities for such partnerships.

Dr. Lloyd said that the Strategic Plan is off to a great start, with many good ideas. He felt that most of the initiatives and strategic goals are designed as multidisciplinary “big science,” not looking to make small, incremental advances but seeking to change paradigms and define the big problems and how to address them, including development of large epidemiologic studies, multiple animal models, high-throughput screening, etc. He said the institute's funding and access strategies must match with initiatives. He said that investigator-initiated P01s have not been available, but that P42 Superfund grants are available, but have been very restrictive, although they may come close to allowing the needed big science. The P30s, with their major investments in cores, address capacity rather than having a research mission, he said. So he felt that as the strategic goals are implemented, there must be a shift in how the research is funded, with new mechanisms to address the big science issues. Otherwise, it could always be the incremental change, with difficulty in communication results or getting access to the databases. Ultimately, he said a paradigm shift in how the research will be funded will be necessary. Dr. Collman said that Dr. Lloyd's ideas would certainly be

part of the discussion as the process moves forward, looking at all of the goals and their implementation, considering not just big science in the extramural community, but in the intramural program as well, with possibilities for synergy between the extramural and intramural programs, taking a “one NIEHS” approach.

Dr. Lloyd appreciated Dr. Collman’s point, but felt that a larger issue is one of access—that there are facilities and cores available at the intramural level that the extramural community has no access to, and that some of the funding mechanisms may be used to reverse those policies and make those resources available to extramural investigators. “If you want to have more robust types of questions being asked by your investigators,” he said, “to be able to get a little bit better access to some of these incredibly expensive [resources] is going to be where a lot of advances are going to be made and huge amounts of insight can be gained.” Dr. Woychik mentioned that DERT is funding several investigators doing nanotechnology research, recognizing that many of them do not have access to nano-characterization facilities, specifically the nano-characterization center at the NCI, and so part of their funding is for access to nano-characterization and standardization resources. Dr. Zeldin said that the question of allowing extramural researchers to have access to intramural facilities is currently “front-and-center” at NIH in terms of opening access to the NIH Clinical Center, and as part of the NCAT’s development. He said it’s a tricky question, with the issue of a prohibition on mixing intramural and extramural funds that would require Congressional action to change. Also, he said, there cannot be a fee for service arrangement, but must be a collaboration. He noted that in the Clinical Center, expanded bench-to-bedside grants with collaborations between extramural and intramural investigators are being funded. He said that NIEHS would love to open access to intramural facilities to extramural investigators, but that the mechanisms to easily do so are not yet in place, other than through collaborations. Dr. Woychik noted that the strategic planning process would spawn creative thinking to help break down the existing barriers.

Dr. Bucher said that specifically regarding high-throughput screening, access for academic researchers in developing new assays and accessing the information being generated had been considered for some time. He said, “I see a future in which much of academic science is going to be able to be done at a computer terminal, with incredibly bright young people looking at large sets of data and answering questions that they have that we wouldn’t even maybe think of, with the resources that we’ve made available.” Dr. Miller noted that one of the challenges of the concept is even having a clear idea of what resources are available at the intramural level. Dr. Zeldin said that the concept is a two-way street, and that there may be resources available in the extramural community of interest to intramural researchers. Dr. Lloyd agreed, but said that a big challenge would be the fact that in many cases the universities themselves have footed much of the bill for establishing facilities, and would be resistant

to opening them to external researchers. Dr. Woychik said that a “good, solid scientific plan” would be the place to start, with encouragement to organizations to participate in collaborative work.

Dr. LeMasters said that she thought the first pillar should be related to the environment, since environment is unique to NIEHS among the NIH ICs. Dr. Woychik explained that all of the pillars are important, and that no one pillar trumps another. He said that fact would be incorporated into the narrative. He said that perhaps Dr. LeMasters’ comment should be included in the mission and vision statements, which define NIEHS and differentiate it from the other ICs. Dr. Newton noted that when the pillars depiction was being developed, it had been difficult to draw the line between the first and second pillars. Since so much research applies to both, it is important to understand that the lines are not hard and fast, she added. Dr. Birnbaum said that was why she liked to think of the concepts as “clouds” as opposed to pillars, since they overlap so much. She also noted that “environment” was prominently mentioned in the definition of the “Fundamental Research” cloud.

Dr. Taylor said that in the current era of budget flatlining, the only way the research could be expanded as envisioned in the plan would be through innovation and technological improvements, along with lack of duplication and increased efficiency through shared resources. Dr. Woychik said that the concept of “one NIEHS” would help, along with looking at the various ICs as “one NIH,” thinking about how to work together more collaboratively. Dr. Birnbaum added that it was not just a matter of increasing efficiencies, but that with the new strategic plan would come some changes in direction, and that to embark on some new ventures, others would need to be closed.

Ms. Hricko said she was troubled that the phrase “environmental justice” had only appeared once in the strategic goals. She also recommended more attention to socioeconomics, and to the concept of place. She agreed with Dr. LeMasters that there should be more emphasis on environmental in the descriptions of the pillars.

Dr. Brody wondered about the role of communications in the strategic plan, specifically whether it would be handled internally or become part of the funding program. She noted the communications challenges posed by the fact that environmental health science has a different political dimension than medical health science. Dr. Collman replied that no element in any of the goals is solely internal or external in nature.

Dr. LeMasters said she felt that the description of the flow of knowledge for Pillar #3, Translational Science, was too narrow. Dr. Birnbaum said that verbiage could be added to note that the research is not a one-directional street. Dr. Woychik said he sees it more as a continuum. Dr. Birnbaum said it is not only a continuum, but is also

interacting circles. Dr. Newton noted that Dr. LeMasters' point is also addressed in Pillar #1.

Dr. Lee complimented NIEHS on what she termed "a masterful distillation of hundreds of ideas." She agreed with Dr. Lloyd that there needs to be a shift from R01 individualized funding mechanisms to multi-center, cross-institutional mechanisms. She felt, however, that there is still a place for traditional, individually based research. Dr. Lloyd explained that he was pointing out that there needs to be an opportunity to implement multi-disciplinary types of investigations, and that currently, funding opportunities for projects such as that are quite limited. Dr. Woychik said that there would be more details about those elements when the implementation strategies are rolled out. He said he did not see the R01s going away, but that under the strategic plan, R01 investigators may identify more opportunities for team science and collaboration with other R01s.

Dr. Conti found the process "phenomenal" and applauded NIEHS for its approach. She said she was particularly excited about Strategic Goal #10 from a state public health standpoint.

At Dr. Birnbaum's suggestion, it was agreed that Council would return to its discussion of the Strategic Plan later in the day.

VI. NTP Office of Health Assessment and Translation Review of Low-level Lead

Rather than the usual NTP update, Dr. Bucher introduced Dr. Andrew Rooney to summarize one particular activity that had been carried out by the Office of Health Assessment and Translation, a recent peer review of a draft NTP monograph regarding low-level lead.

Dr. Rooney said that despite policies that have resulted in significant reductions in exposure and blood lead levels in the US, lead exposure remains a significant health concern for children and adults. Thus, NIOSH had nominated low-level lead to NTP for evaluation. The Draft Monograph on Health Effects of Low-level lead is an overview of the science to date on potential health effects from low-level exposure to lead. The evaluation focused on epidemiological data for health effects at blood lead levels <10µg/dL. That level was chosen because health effects at higher levels are well established, and because the CDC's current definition of elevated blood lead is ≥10µg/dL. The study considered the evidence that neurological, immune, cardiovascular, renal, reproductive or developmental adverse health effects are associated with blood lead levels <10µg/dL. He stressed that the study was not

designed to determine the lowest blood lead level associated with a particular health effect, but rather to look at the evidence that there were health effects associated with a low blood lead level, either <10µg/dL or <5µg/dL. <5µg/dL was often used as a cutpoint for health effects in studies found in the literature. Life stage was considered, as was the presence of data to evaluate the association of bone lead with the health effect, and how that association would compare to the association with blood lead. He defined blood lead and bone lead in more detail for Council, noting that blood lead reflects current exposure whereas bone lead reflects cumulative exposure.

Dr. Rooney presented blood lead level data from NHANES. It showed that mean levels in 1976-1980 were above 10µg/dL, whereas they were below 2µg/dL in the most recent survey, 2003-2008, reflecting decreasing exposures. He noted that the adults in the most recent study were the children in the earlier one, so they at one point had higher blood lead levels and likely had higher bone lead levels due to bioaccumulation.

He said that the monograph included the information that multiple studies had reported significant associations between concurrent blood lead levels <10µg/dL and health effects in adults. The association is supported by consistency across epidemiological studies, and coherence with animal data. He said it is well recognized that the role of early life lead exposure cannot be discriminated from the role of concurrent blood lead in adults without additional long-term studies.

The monograph consists of an Executive Summary, Methods, Exposure, and Health Effects Sections devoted to neurological, immune, cardiovascular, renal, and reproductive and developmental effects. Conclusions are based on primary literature and supported by several other sources of data. The peer review of the NTP Monograph was held November 17-18, 2011 in RTP, with the independent expert panel chaired by Dr. Joel Pounds. The NTP is currently considering the peer review and public comments and will finalize the document in early 2012. The draft monograph's main findings were:

- Both children and adults are vulnerable to the effects of lead.
- There is evidence for many adverse health effects in both children and adults at blood lead levels <10µg/dL and for some <5µg/dL.
- The NTP findings are consistent with and extend what other agencies (ATSDR, EPA) have found in recent reviews.

The NTP considered four possible conclusions for specific health effects in each area—sufficient evidence of an association, limited evidence, inadequate evidence, and no evidence. As an example, Dr. Rooney detailed the NTP conclusion of limited evidence of an association with increased hypersensitivity in children.

He summarized the many conclusions included in the monograph. In terms of major health effects, there was sufficient evidence that blood lead levels $<10\mu\text{g}/\text{dL}$ in adults are associated with adverse effects on renal function, cardiovascular function, and with lower birth weight in women with blood lead levels $<10\mu\text{g}/\text{dL}$. For children with blood lead levels $<10\mu\text{g}/\text{dL}$, the adverse effects included decreased cognitive function (e.g., academic achievement, IQ), reduced growth, delayed puberty, decreased hearing, and increased ADHD and problem behaviors.

Dr. Lee asked about the comparisons used in studies at blood lead levels $<5\mu\text{g}/\text{dL}$; whether they used undetectable levels, or a cut-off point. Dr. Rooney said they had used various different reference populations.

Dr. Hu noted that the report focused on childhood and adult lead exposures, but that prenatal lead exposure as a window of susceptibility of its own is quite large and mounting. He mentioned that there has been a report that early life lead exposures may have an impact on later development of Alzheimer's disease, which illustrates the difficulty of taking a life stage approach when exposures may be prenatal and the outcome may be after 65 years of age.

Dr. Birnbaum agreed that it would be difficult to tease out whether some of the health outcomes seen in old age are the result of bone mobilization and subsequent release of bone lead or the result of programming from early life.

VII. Strategic Plan Process (continued)

Dr. Birnbaum initiated further Council discussion of the NIEHS Strategic Plan. She noted that comments would be accepted through the end of the month.

Dr. Hu, referring to Strategic Goals 8 and 9, asked whether the Strategic Plan included any specific ideas on how to involve more physician-scientists. Dr. Birnbaum said that had been identified as a major issue, but that it would come more in the implementation phase than in the Strategic Plan. Citing the now-discontinued ONES program, she said that NIEHS had been extremely successful in recruiting physician-scientists, and is thinking about other ways to enrich that population.

In the context of how NIEHS is viewed by the public, by leadership at NIH and Congress, Dr. Gasiewicz asked how the Strategic Plan will change the face of NIEHS. Dr. Birnbaum replied that part of that would relate to communications and outreach, along with efforts to work more closely with a variety of partners. Dr. Woychik added that the Strategic Plan is being used as a message for, among other audiences, leadership in other ICs (including his Deputy Director colleagues), particularly bringing

the issue of the environment to their awareness, as well as the importance of prevention. He said that the plan constitutes a document conceived and embraced by the entire EHS community, giving NIEHS the power to take it forward to other ICs, to Congress, and to others. Dr. Maddox, a Deputy Director herself, credited Dr. Woychik's efforts, and posited that a document such as the Strategic Plan does more good for the entire EHS field than perhaps it gets credit for, setting a platform for environmental health research and a needs assessment for the field. Dr. Gasiewicz said he had heard many of these sentiments before, and that the Strategic Plan needs to be a bold statement, going beyond business as usual to help increase funding and identity, and firmly state that the environment has an impact on health and disease. Dr. Birnbaum said his comments would be an excellent suggestion for some of the document's introductory language.

Dr. Taylor stated that success with Congress often came about as a result of being able to relate directly to members' districts or states, or as individuals, such as when disease-oriented institutes could cite a member's family member with a particular condition. He wondered whether NIEHS might be able to employ a similar strategy. NIEHS legislative liaison Mary Gant said that when meeting with individual members, their districts and special interests are always considered. Dr. Taylor said that it must be difficult considering the vast number of districts to be reached by such a small institute. Dr. Birnbaum said that NIEHS relies upon Council members and other friends to help reach specific members of Congress and their districts, since it is inappropriate for her or Ms. Gant to reach out directly to them.

Dr. Winn felt that there should be more of a sense of urgency expressed in the plan, that the time is now and the tools are available. She said a transformative leap could occur.

Dr. Boekelheide praised the strategic planning process and the approach that has been taken. He said "we are in the feel-good phase of the process," but that hard choices will be required in implementation in the face of a flat budget at best. He asked how that process will take place. Dr. Woychik described the next phase, with institute leadership taking the plan to their own divisions and formulating specific implementation plans. Then, those plans will be brought back to Dr. Birnbaum and institute leadership, who will prioritize and ensure good synchrony between the intramural and extramural programs. Then Council will be involved, and the plan will be disseminated. That is "where the rubber meets the road" in terms of recognizing that everything can't be done, he said. He added that he is carefully reviewing the process itself to ensure that the science is still right, that the critical elements of importance to the entire EHS community are being addressed. Dr. Boekelheide thanked Dr. Woychik for his response, and noted that it would be critical to focus resources in order to make measurable advances in different areas. Dr. Woychik agreed, and said that as long as everyone in the community feels

they have been part of the process, they will understand and support the tough choices that will be necessary. He added that in an era of flat budgeting, change management is important. Dr. Birnbaum noted that efforts to increase funding for the community will certainly be continuing.

Ms. Waghiyi, who is a community leader from Alaska, focused her comments on Strategic Goal #5. She described her local area in the northern Bering Sea, its culture, and its environment, where there is a great deal of contamination. She said her people pursue a traditional diet comprised largely of marine mammals, which results in a high degree of cancer. There is also considerable contamination from military activities and global transport of pollutants. Thus, she said, "we are some of the most highly contaminated people on the planet because of where we live." She called for immediate chemical policy reform, and expressed a need to find partners to work to address the human health implications of severe contamination, including health screenings in the small local population of just 800 people. Dr. Birnbaum assured Ms. Waghiyi that the need to address the concerns of underrepresented, disadvantaged communities would be well represented in the Strategic Plan going forward.

Ms. Yeampierre said that Ms. Waghiyi's comments underscored the need to look at regional differences across the country in terms of formulating policies that address the needs of specific communities. She cited the example of expected storm surges in New York City, with no record of the existence or storage of hazardous chemicals in vulnerable areas. She suggested that NIEHS work with EPA and NOAA to address that situation and protect those areas from potential disaster.

Dr. Lloyd praised Strategic Goal #10, which addresses environmental health economics. He said that to ensure funding from Congress, it would be important to effectively tie the financial burdens being faced by the country as a result of exposures to environmental toxicants with the reduced costs associated with a relatively modest investment in research and prevention.

Dr. Hu commented regarding framing. He cited a disadvantaged community his group is working with through their NIEHS P30 Core Center, using GIS modeling to model exposure to oxidative stressors, where they have found an association with food desert neighborhoods and neighborhoods with higher alcohol and tobacco usage. He said that such communities think first about what is increasing disease burden, as opposed to specific problems or institutions. Thus, he said, the NIEHS role in contributing to "a huge insight" into what really increases disease burden must be part of the message in the Strategic Plan. He felt that the current plan does not draw out that message about the large role of the environment in the disease burden. Dr. Birnbaum said that Dr. Hu's comments would help provide some of the needed "punch lines" for the plan.

Ms. Witherspoon suggested that the word “illness” be inserted into the vision statement. Dr. Lee added that the vision statement still needed some subtle wordsmithing.

Dr. Conti said she would like to see the point included that animals also benefit from EHS research and help to inform human health as well – integrating the “one health” concept.

Dr. Lloyd commented on Strategic Goal #8, which addresses education and training. He suggested that it might help for grantees to be required to spend a small portion of their time doing community outreach, such as speaking at high schools. Drs. Woychik and Collman said that was an interesting idea, and that it would be considered.

Dr. LeMasters asked if there is a strategic plan for meeting each Strategic Goal. Dr. Woychik reiterated the next steps he had outlined, particularly the implementation strategies, which will flesh out the details of how the goals will be met. “The Strategic Plan becomes, then, a living framework to help decide what we are going to be doing,” he said. He said the implementation strategies will be brought to Council when they are completed. He said that a well-crafted strategic plan is comprised of operational and financial elements, and that it is that combination that makes a plan come alive, in concert with the broad-based strategic goals.

VIII. Report of the Director, DERT

DERT Director Dr. Gwen Collman updated Council on DERT developments and activities, beginning with staff changes. New arrivals include Dr. Symma Finn, who has joined the Susceptibility and Population Health Branch as a Scientific Program Administrator, Dr. Thad Schug, who has been appointed as a Health Scientist in the Cellular, Organs and Systems Pathobiology Branch, and Barbara Ruffin and Barbara Johnson, who have joined the support staff, working with the Grants Management Branch and the Center for Risk and Integrated Sciences, respectively.

Proceeding to action items stemming from the September 2011 Council meeting, Dr. Collman provided information regarding the citations made to specific grants by grantees in their publications. It had been found that although all NIH-supported investigators are required to cite the grant(s) that have supported their research in all publications, data from 2000 and a more recent analysis showed that this was not taking place – the 2000 rate was approximately 36-57% for EHS Core Center (P30) publications, and 80-85% for R01 publications. In 2011, a sample of P30 grants was analyzed, with an average of 33% citations. She said that there was a need to rely on automated approaches for linking publications to grants, such as that used by PubMed

Central. Also, core center directors will be reminded of the citations requirement at an upcoming meeting.

Dr. Collman also updated Council on the CSR Working Group on the review of EHS applications. This was following up on the presentation to Council in September by Dr. Seymour "Sy" Garte of CSR, to report on the steps he had taken since that time. He convened a working group of EHS researchers in January, who discussed the need for a new Initial Review Group (IRG) for EHS. As a first step toward ameliorating the situation, the committee recommended the chartering of a study section based on the SIEE (Systemic Injury from Environmental Exposures) Special Emphasis Panel, with expanded scope to include most organ systems and limited transitional human studies in environmental health and toxicology, including exposure science. The intention is to bring all EHS grants into one Integrated Review Group, potentially also to include environmental epidemiology/population health studies. Final recommendations are still being developed, and will be presented to CSR and NIH officials for final approval. Once approved, nomination slates will be prepared and the new study section will be operational. The first meeting of the new study section is projected for 2013. "That's a dramatic change in approach and a very positive statement that CSR is really listening to our concerns and is open-minded to trying to rectify some of the problems that we've had," Dr. Collman concluded.

Dr. Collman discussed three changes requested in Council Delegated Authorities as per the FY2011 language. First, a provision for extension of coverage of tuition, travel, and training-related expenses, in addition to stipends, for trainees on T32 grants after the grant ends was added. Second, the item related to provision of supplemental funds for meetings was changed to indicate that supplemental support could be provided for only for grantee meetings or consortia meetings but not for conferences, symposia, or scientific workshops. Third, there was the addition of NIEHS Core Centers (P30) to the provision for authorizing supplemental direct costs, which was correcting an oversight in last year's language. Dr. Gasiewicz moved to approve the changes, Dr. Lloyd seconded, and Council voted unanimously in favor of the motion.

Turning to her 2012 budget report, Dr. Collman described a pie chart depicting the distribution of research project grants (RPGs) in FY2011. Under the research project grants, the average grant size, looking at a mix of mechanism types, was \$402,800. The average of SBIR/STTR grants was \$324,800. Under the Superfund grants, a pie chart depicted the distribution, which includes P42 at 58.2% and the U45 worker training mechanism, at 35.6%.

Turning to competing awards, Dr. Collman noted that in 2011 there were 256 awards made, with a total cost of just over \$74 million. Success rate has improved, with an FY2011 RPGs overall success rate of 14.7%. That compares to a total NIH success

rate of 17.7%. She noted that in 2011 there were many RFAs that received a large number of applications, which would skew the success rate. The R01s success rate in FY2011 was 13.6%, relative to the NIH total of 18.4%. She also shared with Council a list of the RFAs and PARs anticipated in FY 2012, along with a list of several changes in NIH fiscal policy for 2012.

Dr. Collman turned to a discussion of the philosophies and challenges associated with funding decision-making, which she had first presented in 2011. The emphasis remains on funding the highest quality science while supporting the breadth of EHS. There is a desire to maximize support for early stage investigators (ESIs), and NIH now has a mandate to not have preferential funding for them, but to ensure that their success rates are equivalent to established investigators. She said the institute is trying to make the most awards with the available funds, while aligning funding decisions with strategic planning.

In terms of funding decisions, she noted that there is currently no preset pay line, but asked for Council's thoughts about establishing a somewhat conservative (~14-15%) pay line internally along with advertising it to the external community. She proposed identifying pools of money, with 25% going to FOAs, 50% going to unsolicited grants, and the remaining 25% going to Raise To Pay and other special actions. She said that specific criteria would be used to establish priorities within the "gray zone" area, including ESIs, scientific priorities, protecting NIEHS investments, and aligning with the forthcoming NIEHS Strategic Plan. Also, there is a movement toward bringing more Low Program Priority and High Program Priority applications to Council for discussion, particularly in light of the establishment of a pay line.

She also asked for input from Council regarding the idea of defining caps on the large awards, and sticking to them. Those caps could be ≤\$750,000 for human studies and ≤\$500,000 for animal studies. She also requested more discussion on the issue of overall cuts for awards.

Dr. Baylin asked Dr. Collman to comment on DERT's historical funding levels in terms of the ratio of the pool of funding available relative to the application numbers. She replied that DERT receives approximately 750 applications per year, paying in the 18-25% range over the past few years. Although the idea is to go as far down the scoring as possible, it has also been important to consider special areas and Raise To Pays. The scores for NIEHS applications have been spread differently from other ICs in recent years due to some of the review issues, so the pay line has not been set prematurely low. With anticipated improvement in the study section situation, she said the hope is that things will be much more competitive, with the scores competing for a reasonable percentile cut-off.

Dr. Postlethwait asked about the issue of funding young investigators, with the intention of keeping the percentile about the same as senior investigators. Dr. Collman clarified that she meant that the success rate should be about the same. He asked how that would relate to the demographics, and whether that would ensure that enough junior investigators would be funded to replace the seniors as they retire. Dr. Collman said she did not have the answer to that question, but noted that the effort to improve success rates for ESIs with specific targeted numbers stemmed from a perceived problem that not enough were being funded. She said that a good deal of attention is paid to ESIs, including the question of whether to go ahead and pay them or send them again through review, for that experience.

Dr. Postlethwait commented that the \$500,000 cap on non-human studies would probably preclude NIEHS from doing any primate work. Dr. Collman said that had been discussed, and said that DERT could come up with a more appropriate cap for primate studies if it was felt that they needed to be treated differently. Dr. Birnbaum noted that the questions being asked of Council are areas where the external input is needed. Dr. Collman said that in the case of investigators with multiple grants totaling more than \$1.5 million that will trigger special action consideration as well.

Dr. Hu asked whether applications exceeding the \$500,000 cap tend to be cross-disciplinary, multiple-PI projects requiring considerable resources. Dr. Collman said that a deep analysis had not been done, but that her feeling is that they are not.

Dr. Phan asked whether DERT was considering re-balancing its portfolio to maintain its current level of R01s. Dr. Collman said that with the emerging strategic plan and its implementation, the mix will be under consideration, and leadership will need to decide how to best program out the different categories.

Dr. Boekelheide asked about the idea of instituting a preset pay line. He said that transparency and communication with the body of investigators would be very important. He asked whether the pay line would be real and enforced. Dr. Collman said that in the past, interested parties were not told about the pay lines until the year after the file is frozen – retrospectively. She said that establishing the open pay line would not change internal practices substantially, but would send a different message to the community and allow them to plan more accurately. Dr. Boekelheide said he would strongly advocate going forward with the idea. He also commented about the proposed cap on non-human research, noting that other research in that area can be quite expensive, such as Next-Gen sequencing and bioinformatics. He said that as a result the cost differential between human and non-human research is becoming blurred. Dr. Collman said that most of the studies incorporating those newer technologies are in the human category, but that if need be the caps could be reconsidered if the strategy seemed inappropriate.

Dr. Lloyd said he felt that aggressively advertising a conservative pay line would be very positive, given the fact that that pay line would still be much higher than those advertised by several other ICs, and would likely attract researchers to EHS. He recommended maintaining a multiple percentile cushion in terms of the advertised pay line. He and Dr. Collman agreed that the referral assignments would be key.

Dr. Postlethwait asked about the idea of earmarking money for specific categories, wondering how the ~25% spending figure for RFAs compares to other institutes, and how it can be assured that what is being funded is good science. Dr. Collman replied that this would be a target, but if the quality of the work does not meet expectations, there is no pay out “just because.” Dr. Maddox estimated that approximately 15% of NICHD funding goes into classic RPGs. Dr. Winn did not know the number immediately for NCI, but promised to provide it later.

Dr. Postlethwait was excited to hear the prospect of a study section or IRG chartered to EHS, noting that it has been tough to get EHS grants through CSR in the past. Dr. Collman agreed that it will be a big improvement. Dr. Birnbaum said NIEHS has been working on the issue for many years, and that the recent change in leadership at CSR has put the situation on the right track.

Regarding the set cuts for all awards, Dr. LeMasters said she would recommend an exception for modular grants, since even a 10% cut would be “very impairing.” Dr. Collman mentioned that another model that had been discussed would be based on using priority scores as a metric for cuts. Dr. Boekelheide said he did not think that was a good idea. Dr. Gasiewicz agreed, and felt that cuts should be made on a case-by-case basis. Dr. Collman said it is done on an across-the-board basis, but that they are sensitive to case-by-case considerations as they arise, and program staff do work closely with investigators to determine whether a cut may be very damaging to a grant. She said that ultimately, they try to be fair.

Dr. Lloyd said that 10-20% set cuts would dampen investigators’ enthusiasm, and would send the wrong message in terms of getting the best science out of the institute. Dr. Finnell said he strongly disagreed with Dr. Lloyd, because study sections vary so widely. He agreed with the current approach – having across-the-board cuts, but being cognizant of case-by-case situations. Dr. Collman said it would be important to avoid the perception of the process being subjective or arbitrary.

IX. Consideration of Grant Applications

This portion of the meeting 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).

X. Concept Discussion: Microbiome/Environment Interactions

Prior to the concept clearance presentation, Dr. Collman welcomed another new Council member, Dr. Andy Kramer from the Duke Nicholas School for the Environment.

Dr. Lisa Chadwick from DERT presented information on the interaction of the microbiome and environmental stressors and a proposed research program in that area.

She defined and described the microbiome, along with the emerging understanding of the role of the microbiome in a number of elements of human health. She said that the microbiome is so important it is sometimes referred to as our “11th organ system.” There is considerable diversity in the microbiome, whether on the skin or in the gut or the lungs. The NIH Common Fund has supported the Human Microbiome Project, which has characterized the microbiomes in five anatomical areas – nasal, oral, skin, gastrointestinal, and urogenital.

Research interest in the microbiome has grown recently due to emerging knowledge about association of changes in the microbiome with a variety of diseases. For example, it has been reported that lean individuals have a more diverse microbiome than obese individuals. It has also been seen in experiments in mice that the gut microbiome can have a systemic effect, impacting brain development and behavior.

Regarding why this area is of interest to NIEHS, Dr. Chadwick said that the microbiome has been shown to be very sensitive to external influences, resulting in the question: if diet and drugs affect the microbiome, what about environmental toxicants? Very little is currently known about those interactions, but at least one study showed that exposure to an environmental toxicant can affect the composition of the microbiome. There is also interest because it is known that the microbiome can metabolize environmental toxicants, including into more toxic forms. This may represent a new paradigm for environmentally induced disease. In one scenario, a population exposed to an agent would have their own slightly different microbiomes, which would metabolize the toxicant differently, leading to different internal doses and different disease outcomes. Also, a population suffering a developmental exposure to a toxicant may find its microbiome composition altered, potentially leading to disease.

The proposal is to develop a research program designed to investigate the interaction between the microbiome and the environment. It encompasses two proposed PARs:

1. *Environmental Influences on the Microbiome* (R21)

- How does exposure to environmental chemicals affect the composition/function of the microbiome?
- How stable are these changes?
- How does the developmental timing of exposure affect this?

2. *Metabolism of Environmental Toxicants by the Microbiome* (R21, R01)

- How does the microbiome metabolize environmental toxicants?
- How does this impact internal dose?
- What environmental chemicals are metabolized in this manner?

Dr. Chadwick noted that the PARs would not accept studies investigating diet, probiotics or pharmaceuticals.

Dr. Lee was the first Council reviewer. She noted that the microbiome is a hot topic in science currently, and having consulted the literature to familiarize herself with it, she predicted an exponential rise in papers related to it. She said there is significant impact and relevance to EHS, and it would be a good area for NIEHS to get into as it is developing. She said that the microbiome/environment interaction represents a complex new way to look at toxicity. She noted that the timing of events would be a critical element to be examined. In developing and releasing the PARs, she recommended timing them to the release of the Human Microbiome Project data, so that those extensive resources could be tapped into. Dr. Chadwick pointed out that all of that information was already available.

Dr. Finnell was the second Council reviewer. He agreed with Dr. Lee that timing of the program would be important. With the precipice of 2013 budget uncertainty, he wondered whether it would be wise to issue new RFAs that would invite more grants and potentially flood the system "for something that doesn't seem to be absolutely compelling now when we could wait a couple of years for more development of microbiome big projects and build on that." He said there didn't seem to be any rush, and that he favored going slow sometimes on releasing RFAs.

Dr. Chadwick pointed out that the proposal was for a PA, not an RFA, so there would be no money set aside for it. She also felt that this is the time to start the program, with the Microbiome Project wrapping up and its data largely available. She noted that other ICs such as NIDDK and NICHD have microbiome-related projects underway. She predicted that this area would be very important for environmental health also, so it would be

advisable to stimulate research activity now rather than later. Dr. Birnbaum added that this was a good example of one of the new directions envisioned in the new strategic plan: "I personally see this as an area into which we have to move, because it is likely to have very, very important consequences for our ability to prevent illness, disease and disability from environmental exposures," she said.

Dr. Winn expressed concern that with a variety of smaller grants, there may end up being "a motley collection" of different chemicals, types of people, or animals being studied. She suggested consideration of methodologic ground rules to establish some control. She said it was probably premature for standardization, but that it might be possible to establish some guidelines at this point. Dr. Chadwick thought that was an excellent suggestion.

Dr. Chesselet suggested that it would be important to specify the dietary context for experiments, to ensure that experimental animals would receive consistent, well-documented diets.

Dr. Postlethwait said that if this was to be released as a PA, he would be concerned about involvement of people with the appropriate scientific expertise in the review process. Dr. Chadwick said that was one reason for the PAR – so that there would be more control over the review.

Dr. Lloyd asked if potentially the program would be restricted to the gut microbiome versus the skin or others, which would help to limit the scope of applications. He noted that if pyrosequencing is employed, it would not be an inexpensive proposition. He asked Dr. Chadwick whether the likely experimental procedures had been assessed in terms of the costs involved. She said that issue had been discussed frequently by the working group, and that they wished to raise the funding caps and allow three years for the project as opposed to two. Dr. Lloyd also wondered whether the program could take advantage of existing primate studies, in that the rodent models may not mimic human outcomes. Dr. Chadwick said that although she would anticipate most of the applications to involve the gut microbiome, lung and skin would also be important as other first points of contact with environmental chemicals. She noted also that many of the rodent model studies start with a germ-free animal with subsequent introduction of a human microbiome. She said that so little is known in this area, starting with animal models would still provide useful information, later moving to human studies. She said she was unaware of many primate microbiome studies at this point. Dr. Lloyd noted that starting with germ-free animals is not trivial and can be costly.

Dr. Hu noted that very little is known currently about the methodology of how to study the microbiome in humans. He said he would encourage that the RFA be written in such a way that the challenges involved in the human studies are clear to researchers.

Dr. Chadwick said that the Human Microbiome Project has established many of the methodologies and standards, but that it would still in fact be challenging.

Dr. Taylor felt that this would turn out to be a very long-term project, more like a five-year project than a two- or three-year project. He said it was a perfect example of the possible two-way street between institutes to coordinate and collaborate, but in the absence of collaborations, going it alone would be a mistake. Dr. Chadwick said there had already been some interest from NICHD. She said that looking at the issue in a more systemic way is actually a strength of NIEHS in this area. Dr. Maddox added that interest from NICHD would depend on how the RFA is written, and that they would be interested in the microbiome with respect to prematurity, in that premature births are the number one priority currently at that institute.

Dr. Collman called for a motion and vote to approve the concept, which is written broadly. Approval would allow DERT to continue to develop the concept. Dr. Lee moved to accept the concept. Dr. LeMasters seconded. Council voted unanimously to approve the concept, except for an abstention by Dr. Finnell.

XI. The FDA/NIH Tobacco Initiative

Dr. Robert Croyle, Director of the Division of Cancer Control and Population Sciences at NCI, briefed Council on the most recent developments related to the NIH/FDA partnership in tobacco regulatory science. He updated Council on the FDA and the Tobacco Control Act, the authorities and goals associated with the Tobacco Control Act, and associated funding opportunities and initiatives. He characterized the program as a major new source of research funding.

He went over some of the data regarding tobacco use in the US, including the overarching fact that it is still the leading preventable cause of disease and death in the nation. FDA was granted the authority to regulate tobacco products under the Family Smoking Prevention and Tobacco Control Act, which was signed into law in 2009.

One element of the FDA's authority under the act is to conduct research to support tobacco product regulation. Tobacco product regulation is 100% funded by user fees from the industry, and by law those funds may not be used for any other purpose. In the FY 2012 budget, that amount is approximately \$500 million, with the FDA tobacco budget rising to an estimated \$712 million in FY 2019.

Dr. Croyle noted that a strong science base is a precondition to successfully regulating tobacco products, including setting tobacco product standards, identifying biomarkers to

tobacco-associated pathogenesis and disease, and developing, implementing and evaluating tobacco product advertising and marketing standards.

The first major study funded under the Act is the Population Assessment of Tobacco and Health (PATH) Study, with the FDA providing \$125 million over five years to NIDA for a national longitudinal cohort study involving more than 40,000 tobacco users. When datasets emerge from the PATH Study, there will be opportunities for follow-up research.

Dr. Croyle reported that FDA, CDC and NIH have been working together to prepare a number of funding opportunity announcements relevant to the FDA's new authority. The first FOA released was to support Competitive Revisions (R01 and U01), with NCI, NHLBI, NIDA, NIEHS, and NIMH as the participating ICs. It will fund an estimated 20 awards at a total of \$10 million per mechanism for FY 2012. All announcements and grants must be vetted by FDA to ensure that they conform to the authority granted under the Act. FDA will approve the funding for the Competitive Revision proposals by August 2012. Also released was an announcement of Administrative Supplements to Program Project/Center Grants, as P01, P50 and P60 grants, providing \$40 million in funding over two years, with NCI as the lead IC. Those awards are expected by September 2012.

Beyond the current supplements, which can be accomplished quickly, additional funding mechanisms for the out years are being developed. They include a recently-announced notice of Intent to Publish an RFA funding Centers of Excellence (P50) on tobacco regulatory science, which will be awarded in September 2013. Also under consideration are Training Awards (K, T, F and/or R) to help build and broaden scientific expertise in the tobacco regulatory science. NIEHS is taking the lead on that concept. Dr. Croyle also described several other concepts currently under consideration associated with this major effort to ramp up in tobacco regulatory research.

Dr. Lloyd asked whether there was any data on the impact of the graphic tobacco product warning labels currently in use in Europe in terms of impact on new smokers or quitting smokers. Dr. Croyle said there were international studies in progress on that question, and the evidence is coming in. He said that initial data indicated an impact on awareness, knowledge and intent to quit, but that there was not much evidence so far on the fundamental surveillance questions such as incidence, mortality, and prevalence. He said that the initial evidence on cognitive belief and attitude has been "quite promising." He added that the US cigarette pack would also have a National Quit Line number.

Dr. Taylor asked whether the source of the funding was already set, citing previous experience with state-level tobacco settlement money being diverted to other pursuits.

Dr. Croyle said that by statute these funds could not be diverted, and in fact the purposes for which the funds can be used are stated quite explicitly. For example, he said, even smoking cessation trials would be outside the purview and would not be funded, because the specific focus is on the product itself.

Dr. Birnbaum asked whether research on secondhand smoke, particularly given new types of tobacco products, would be acceptable. Dr. Croyle said that it would, given that the research centered on any health claim for a product. He noted that this is the first bill that grants FDA authority on a population level, as opposed to the individual level, with a public health standard in review of products.

Dr. Birnbaum asked whether the tobacco industry has any control over the use of the funds. Dr. Croyle replied that it has no influence over how the funds are expended, other than possibly through litigation over how FDA is exercising its authority. Dr. Birnbaum said that it will be important to actively communicate that, so that researchers will not be uncomfortable about accepting the funding in terms of its association with the industry.

Dr. Postlethwait asked whether the anticipated increase in funding would be attributable to increases in user fees, or an implicit assumption that the research efforts would not contribute to a reduction in tobacco use. Dr. Croyle agreed that taxing a product that you are trying to reduce use of creates a conundrum, but said that the projected increase is tied to projected user fee revenues, with some delay in how they accumulate. He said that of course the long-term public health goal is to reduce tobacco use in the US.

In response to a question from Dr. Hu, Dr. Croyle noted that the studies under the Act are not limited to new products, but that they are receiving much of the attention due to the fact that the products have changed substantially over the past few years.

Ms. Yeampierre opined that the graphic warning labels would be ineffective in discouraging young people from using tobacco products, and wondered how they might be engaged with messages that will resonate with them. Dr. Croyle noted that the warning labels were the product of substantial research in many different sub-populations. He said that in terms of impact, they will probably only account for a small variance, among many other anti-smoking campaign elements.

Dr. Collman noted the NIEHS leadership in the training initiative Dr. Croyle had described, with an internal team working on the effort. She asked for input from Council members who have a history of tobacco-related research to help determine the appropriate training capacity.

XII. Trainee Tracking at NIEHS

Dr. Christie Drew of the Program Analysis Branch briefed Council on a newly developed method for tracking trainees, called CareerTrac.

There are several reasons to track trainees and assess their long-term career outcomes. First, there are elements of accountability, such as the Government Performance Results Act, provisions of the NIEHS Strategic Plan, and the fact that T32 institutional training grants require tracking for ten years. Also, having outcome data can help with knowing where trainees go, improving existing programs, planning appropriate workforce levels, and understanding attrition rates.

Prior to CareerTrac, it was difficult to track trainees – data were not searchable or usable for aggregate analysis, and the existing module only looked at a narrow window of success, yielding incomplete information.

CareerTrac was initially developed from 1999 to 2008 by Fogarty International Center (FIC). NIEHS adapted and enhanced the FIC system through 2010. Phase 3 in FY 2011 saw a multi-tenant system instituted, hosted at NIEHS. Phase 4, in FY 2012, will involve pilot testing, new partners, and improvements to the system, with first full data expected. The system is the result of a partnership between NIEHS, FIC and the contractor Open Intelligence.

CareerTrac is designed to provide a structured database to inform about where trainees are now, and what they have accomplished based on the training they received. It improves access to existing data, allowing tracking of trainees by T32 PIs for more than ten years. It automates trainee tracking for PIs, and allows them to retain data over time. It also automates key information they need for progress reports and renewals. CareerTrac offers a web-based interface for PIs and their designees for entry of trainee accomplishments. There is a robust reporting structure focusing on the trainees of the three current tenants – FIC and NCI (~5000 trainees), NIEHS T32s (~4100 trainees) and NIEHS Superfund (~1000 trainees). It does not duplicate existing resources, but wherever possible, it will extract data from existing sources. It employs a role-based access, with PIs only seeing trainees in their programs, but with program officers able to see everything. It is designed to minimize work for PIs and provide incentives for its use, and to retain trainee information beyond the life of the grant. Ultimately, it is intended to balance flexibility with structuring of the data.

Dr. Drew went over the data sources in use to populate CareerTrac. She also shared several screen shots from CareerTrac that depicted examples of the types of data that are available, navigation, search capabilities and other features. She also shared an initial look at the output of CareerTrac in terms of being able to analyze where trainees are now.

Future analyses under development will include metrics of length of training, number and type of academic degrees received, number of trainees per mentor, mentors/number of trainees/accomplishments, and several more.

Currently, T32 pilot testing is underway, with data being imported and reports being developed. Enhancement efforts are ongoing. Also, there is an effort to bring in new tenants, including NIEHS DIR/IRTA Fellows and trainees from other ICs. There has been interest from NIGMS, NCI, NHLBI, and NINDS thus far.

Eventually, it is hoped that later phases will allow direct trainee access, a potential interface with the NIH Commons system, more partners, and additional mechanisms in the system.

In summary, Dr. Drew listed the value added by CareerTrac:

- Structured data: for the first time, we will know
 - Who is being tracked
 - Where they end up
 - What they have accomplished
- Ability to analyze data that can help inform decisions
- Ability to leverage existing IMPAC II information
- Database for PIs over time
- Automated tracking reports needed for progress reports and renewal applications
- Data framework and application code that is fully scalable

Dr. Chesselet said she understood that NINDS had put a lot of effort into designing a similar system, and asked Dr. Drew how she and her team had ensured they were not duplicating those efforts. She was under the impression that NINDS had received considerable pushback from ICs that did not want to use external systems. She understood that it had originally been developed to track performance with training of underrepresented minorities and genders, but that the information was not to be put into the system without release from individuals. Dr. Chesselet described other complications regarding reporting. Dr. Drew said that OMB had approved CareerTrac to collect minority and gender-related data. She said that there need to be conversations about some of the issues raised by Dr. Chesselet at a much broader NIH level.

From a community-level perspective, Ms. Yeampierre noted that there are many groups working quite hard to get young people of color interested in math and science, and pointed out that use of the word “diversity” has watered down efforts to address the effects of past discrimination. She would like to find out specifically about efforts to involve groups that have been historically excluded, such as African-Americans, Puerto

Ricans, and Mexican-Americans. She would like to see those efforts to attract and retain such candidates documented and reported. Dr. Drew agreed, but pointed out that to track those things there must be categorization, which is delicate.

XIII. The Environment, Genetics and Age: The Ménage à Trois of Autoimmunity

Dr. Fred Miller, Acting NIEHS Clinical Director and Chief of the Environmental Autoimmunity Group presented a comprehensive summary of the state of the science in autoimmunity, including a look at the work of his group related to environmental autoimmunity. He reported that autoimmune diseases are a growing public health problem, with more than 80 disorders affecting more than 22 million Americans and increasing prevalence of unknown causation. There is considerable evidence that the environment plays a role in the pathogenesis of autoimmune diseases, in the form of both infectious and non-infectious agents. There is also evidence that genetics and gene-environment interactions result in autoimmune phenotypes, and that aging factors in as well, as prevalence of autoantibodies and autoimmune diseases increases with age. Dr. Miller described the Environmental Autoimmunity Group, which is the only NIEHS scientific unit located in Bethesda, in order to utilize the unique resources of the NIH Clinical Center. Much of the group's research has focused on myositis as a model autoimmune disease, exploring the pathogenic mechanisms involved and which specific gene-environment-age interactions lead to which specific clinical syndromes.

XIV. Immunotoxicity Outcomes in a Population Exposed to Marine Contaminants

Dr. Philippe Grandjean of the University of Southern Denmark and the Harvard School of Public Health presented a summary of a portion of his work to Council. He is a longtime NIEHS grantee whose work has focused on environmental epidemiological studies of a series of birth cohorts in the Faroe Islands, an isolated fishing community in the North Atlantic Ocean. Due to its seafood-oriented dietary habits, the population is heavily exposed to marine contaminants such as methylmercury, PCBs and PFCs, and Dr. Grandjean researches potential impacts on neurotoxicity, growth and development, immunotoxicity and endocrine disruption. He presented data from the Faroe Islands cohorts that documented an association between methylmercury exposure and adverse neurodevelopmental effects, including negative impact on IQ, along with statistical analysis that suggests underestimation of the methylmercury effects. He also shared

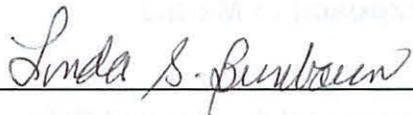
results of his research on immunotoxicity. One study showed that the higher the PCB exposure, the less efficient the response to childhood immunization, a concept that could have far-reaching implications for the impact of environmental exposures on variability in responses to vaccines. Studies of exposures to PFCs, both maternal and in childhood, showed similar effects on vaccine response, adding to the evidence of immunotoxic effects. He described what he called a "silent pandemic" of IQ losses and other neurotoxic effects, immunotoxicity and endocrine disruption resulting from exposures to lead, mercury, PCBs, and other toxicants.

XV. Adjournment

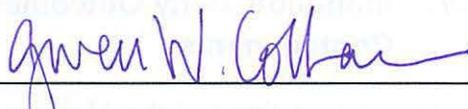
Dr. Collman thanked Council for its efforts and officially adjourned the meeting.

The meeting was adjourned at 12:18 pm on February 16, 2012.

CERTIFICATION:



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