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

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

May 14-15, 2013

The National Advisory Environmental Health Sciences Council convened its one hundred thirty-ninth regular meeting on May 14-15, 2013 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 May 14, 2013 from 8:30 a.m. to 5:00 p.m. In accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), the meeting was closed to the public on May 15, 2013 from 8:30 a.m. to 12:00 p.m. for consideration of grant applications. Notice of the meeting was published in the *Federal Register*.

Council Members Present

Kim Boekelheide, MD, PhD
Julia Brody, PhD (by telephone)
Kelley Brix, MD (by telephone)
Marie-Francoise Chesselet, MD, PhD
Vivian Cheung, MD
Lisa Conti, DVM
David Eaton, PhD (ad hoc)
Thomas Gasiewicz, PhD
Tomás Guilarte, PhD (ad hoc)
Andrea Hricko, MPH
Howard Hu, MD. MPH, ScD (by telephone)
Norbert Kaminski, PhD (ad hoc)
Randall Kramer, PhD
Mary M. Lee, MD
Yvonne Maddox, PhD (*ex-officio*)
Linda McCauley, PhD, RN (ad hoc)
Edward Postlethwait, PhD
Viola Waghiyi
Deborah Winn, PhD (*ex-officio*)

NIEHS Staff

Joel Abramowitz, PhD
Kathy Ahlmark
Bruce Androphy, JD
Joellen Austin
John Balbus, MD
David Balshaw, PhD
Martha Barnes
Linda Bass, PhD
Sharon Beard
Linda Birnbaum, PhD
Wanda Boggs
John Bucher, PhD
Matthew Burr
Danielle Carlin, PhD
Lisa Chadwick, PhD
Sandra Chambers
Pamela Clark
Jennifer Collins
Gwen Collman, PhD
Allen Dearry, PhD
Christina Drew, PhD
Dorothy Duke
Donald Ellis
Benny Encarnacion
Symma Finn, PhD
Christine Flowers
Mary Gant
Stavros Garantziotis, MD
Barbara Gittleman
Kimberly Gray, PhD
Astrid Haugen
Michelle Heacock, PhD
Jerry Heindel, PhD
Heather Henry, PhD
Michael Humble, PhD
Evan Johnson
Laurie Johnson
David Kinnamont
Annette Kirshner, PhD
Cindy Lawler, PhD
Chris Long
Robin Mackar
J. Patrick Mastin, PhD
Kim McAllister, PhD
Steven McCaw

Rose Anne McGee
Liz McNair
Aubrey Miller, MD
Sri Nadadur, PhD
Sheila Newton, PhD
Aaron Nicholas
Liam O'Fallon
Jerry Phelps
Nicole Popovich
Molly Puente
Ericka Reid, PhD
Leslie Reinlib, PhD
Elizabeth Ruben
John Schelp
William Schrader, PhD
Thad Schug, PhD
Wynonah Sessoms
Daniel Shaughnessy, PhD
Carol Shreffler, PhD
Jordan St. Charles, PhD
William A. Suk, PhD, MPH
Kimberly Thigpen Tart, JD
Claudia Thompson, PhD
Sally Eckert-Tilotta, PhD
Frederick Tyson, PhD
Christopher Weis, PhD
James Williams
Leroy Worth, PhD
Rick Woychik, PhD
Darryl Zeldin, MD

Members of the Public Present

Maureen Avakian, MDB, Inc.
Deborah Bittman, SSS
Laura Bono, SafeMinds (representing NIEHS Partners)
Rich Cohn, SRA International
Ernie Hood, Bridport Services
Pia MacDonald, PhD, SSS
Richard Morris, PhD, SRA International
Michael Phillips, RTI International
James Ter Maat, SSS
R. Thomas Zoeller, PhD, University of Massachusetts, Amherst

I. Call To Order and Opening Remarks

NIEHS/NTP Director and Council Chairman Dr. Linda Birnbaum welcomed attendees and called the meeting to order. She asked all present in the room to introduce themselves, which they did. She mentioned that Council members Dr. Julia Brody and Dr. Howard Hu would be attending by telephone. She welcomed new Council members Drs. Eaton, Guilarte, McCauley and Kaminski, and noted that Council members Elizabeth Yampierre, J.D., Dr. Thomas McKone, and *ex officio* member Dr. Jennifer Orme-Zavaleta were not present at the meeting.

II. Review of Confidentiality and Conflict of Interest

NIEHS Director of the Division of Extramural Training and Research and Designated Federal Official Dr. Gwen 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 February 2013 Meeting Minutes

Approval of the February 2013 minutes was moved and seconded, and Council voted unanimously to approve the minutes. Dr. Collman noted the dates of the upcoming Council meetings for members to put on their calendars.

IV. Report of the Director, NIEHS

Dr. Birnbaum updated Council on institute developments since the February 2013 Council meeting.

Implementation of the new NIEHS Strategic Plan continues. Institute leadership is currently reviewing reports from the cross-divisional teams that were formed to address needs in eight areas: epigenetics, inflammation, stem cells, the exposome, predictive toxicology and disease, global environmental health, knowledge science and data management, and the website and social media. Leadership is close to finalizing directions for how to go forward in those areas.

Dr. Birnbaum reported on progress of the NIEHS Nano GO (Grand Opportunity) Consortium, which was formed in 2009 with 13 grants funded by ARRA. One of its goals was to carry out round robin experiments across different labs to standardize assays for predicting toxicity of nanomaterials. Efforts were focused in two integrated interlaboratory initiatives, one concentrating on *in vitro* cytotoxicity and inflammatory responses to engineered nanomaterials; the other assessed rodent pulmonary responses to engineered nanomaterials.

Dr. Birnbaum reported that the institute had entertained several special visitors in recent months, including NIH CIO Andrea Norris, NINDS Director Story Landis, NIDDK Director Griffin Rodgers and EPA Assistant Administrator Gina McCarthy (who has been nominated to be the new EPA director) and Janet McCabe, Deputy Assistant Administrator of the EPA Office of Air and Radiation.

Regarding budgetary considerations, Dr. Birnbaum noted that although the institute's FY 2013 budget would have been relatively flat under the full-year continuing resolution (CR) passed earlier in the year, with the across-the-board budget cuts generated by sequestration, which took effect March 1, substantial cuts have been made. Intramural programs (DIR and DNTP) have been cut 4.6-4.7% and the grants program has been cut 5.7%, with about 30 fewer grants being funded this year than had been anticipated. The Superfund program was cut by 5.1%, reflecting the across-the-board reduction. The NIEHS/DOE funding has been reduced from $10 million to $9.23 million due to sequestration. She said that due to the soft hiring freeze in effect over the past two years, no federal staff members have needed to be furloughed as a result of the sequestration, although there has been some impact on contracts and contractors. She mentioned that the President's FY 2014 budget request reflects a slight increase over the FY 2012 appropriation (before sequestration), but that the President's budget is "dead on arrival," with a real possibility of another CR being necessary in October, along with the potential for additional sequestration cuts in 2014. She also summarized recent legislative activities, including several Congressional hearings and briefings.

Dr. Birnbaum briefly summarized several recent scientific advances involving publications by NIEHS/NTP personnel or grantees. She described NIEHS participation as a founding partner in the National Consortium for Data Science, a government/academic/industry partnership started in the Research Triangle area to focus on accessibility to "big data" and training the next generation of information specialists. She reported on recent outreach efforts and community forums, including a visit she had made to Indian Country in New Mexico, a community forum held in Seattle at the Duwamish Superfund site, and a Detroit community forum.

She reported on recent developments related to training and science education, and provided a rundown of recent meetings and events and upcoming meetings. She enumerated several awards and recognitions given to NIEHS employees and grantees over the past few months.

Concluding her presentation, Dr. Birnbaum briefed Council on the President's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, which involves an FY 2014 Federal investment of $110 million (including $40 million from NIH) and a further $122 million investment from private partners.

Dr. Kaminski asked Dr. Birnbaum whether the NIH's $40 million for the BRAIN initiative would be new money. She replied that it was in the President's budget for NIH, so it would represent new money for NIH.

Ms. Waghiyi encouraged Dr. Birnbaum to visit and conduct a community forum in Alaska, where there are 231 Federally recognized tribes, with some of the most highly contaminated populations on the planet due to their reliance on traditional foods. Dr. Birnbaum promised to investigate the possibility of doing so, but that it would be unlikely this year due to budgetary constraints.

Dr. Eaton asked Dr. Birnbaum to put the "30 less grants than anticipated" into the wider context of the total number of grants. She replied that non-competing grants and training grants were not being cut, and that the number she had provided would apply to Research Project Grants (RPGs). Dr. Collman clarified that the number of grants was reduced from 153 to 133, for a loss of 20 grants.

V. Report of the Director, DERT

DERT Director Dr. Gwen Collman updated Council on DERT developments.

She described DERT's implementation of the new NIEHS Strategic Plan. DERT has created 11 strategic planning teams as the division strives to closely align its activities with the plan.

Part of that effort has been an initiative to benchmark the current research investments, so that over time it will be possible to compare how the portfolios change and grow in different ways along with the strategic planning ideas. With this new approach to analyzing the portfolio, a contractor is in the process of coding all 1500 current grants (more than 1000 have been coded to date) to depict their alignment with strategic plan goals and subgoals.

Another element of the campaign to align DERT activities with the strategic plan is a proposed reorganization of the division. Under the proposal, the division's programmatic areas would be re-worked. The Worker Education and Training Branch and the Program Analysis Branch would remain as they are, and four new branches would be created: a Genes, Environment and Health Branch, an Exposure, Response, and Technology Branch, a Population Health Branch, and a Hazardous Substances Research Branch.

A public webinar will be held on the proposed DERT reorganization on June 6 at 12pm for additional public comment and input. In the meantime, questions or comments can be emailed to DERTpublicmeeting@niehs.nih.gov.

Dr. Kramer endorsed the reorganization plan, and asked about the strategic plan theme of health disparities and global environmental health. He said it obviously played out in association with the proposed Population Health Branch, but wondered if it would associate with the other branches as well. Dr. Collman said that the strategic plan implementation teams that had been stood up by DERT worked across any branch boundaries, with membership from all of the business areas in each of the goal areas. She said that the themes mentioned by Dr. Kramer cut across several different areas, and constitute one of the NIEHS cross-divisional areas, where much work has been conducted. Thus, there will be considerable opportunities for cross-divisional partnerships and synergies regarding those issues, although they will not be housed specifically within a branch.

Dr. Boekelheide approved of the retrospective analysis approach described by Dr. Collman, as it sets in place a programmatic method of looking forward. He asked if a next step might be weighting by goal. Presumably that would have been an ad hoc process in the past, he observed, but now it could be proactive. He asked Dr. Collman if there had been any thought given to that concept, the implications of which would be big. Dr. Collman noted that strategic goal priority areas are already being used as a mechanism for specials and raise-to-pays. She asked for Council's input on the idea of weighting, to help prioritize in terms of the scientific opportunities and the need to bolster investments in certain areas, including the balance of research investments in the long term. She said that the absolute measure of how big the portfolio should be in any one area is a very difficult task, and she looks to Council for guidance on that.

Dr. Mastin related an email inquiry from Ms. Karen Miller. She asked about funding for translation through the centers program, particularly BCERP, and whether the Research to Action funds are still available. Dr. Collman noted that the analysis she had presented did not include any of the multi-project programs, except for individual U01s. The Breast Cancer and Environment U01s were part of the chart. She said that they align with Strategic Plan Goal #2, individual susceptibility and the lifespan. As the program enters its final years, science planning will take place for next steps related to the breast cancer and the environment portfolio. Under the Partnerships for Environmental Public Health, the Research to Action program has been announced via a Program Announcement, and those opportunities, which align with Strategic Plan Goal #6, are still available.

Dr. McCauley asked about DERT portfolio alignment in terms of translational research. Dr. Collman replied that throughout the strategic planning process, prevention had been a major theme in terms of determining the priorities for the next five years. There was much discussion about translation in the context of prevention and exposure reduction, moving to interventions at the population level. She noted that that type of science has been difficult to support extramurally at NIEHS given limited funding, with no large

portfolio of clinical trials of strategies for exposure reduction. It is, however, an area that is part of the implementation plan, in different areas where it makes sense. Dr. McCauley mentioned that looking at the CTSA awards, there are environmental health scientists coming from schools of public health who are involved in those initiatives. Dr. Collman said that opportunities for translational partnerships with other NIH institutes had increased in recent years, with ICs often coming to NIEHS to ask for collaboration on environmental factors.

Ms. Waghiyi asked Dr. Collman to elaborate about the community-based intervention and prevention aspect of the Population Health Branch, particularly as it relates to public health research involving environmental health disparities and environmental justice. Dr. Collman said that one of the main goals of the reorganization is to take what already exists within the portfolios and create more focused organizational units to promote those ideas. She noted that existing programs such as Partnerships for Environmental Public Health and Research to Action would be housed in a group with a focus on intervention, prevention, health disparities and environmental justice. The change does not create new specific funding opportunities *per se*, but is designed to bring staff together to more deeply engage in such program areas.

Responding further to Dr. McCauley's question, Dr. Birnbaum said that part of the issue is the difference between the medical model and the public health model, with it being a challenge to get clinically focused people to move into the public health arena.

Dr. Lee asked whether reconfiguration of staff would result in shifts of grants assigned to particular people. Dr. Collman said that clearly there are staff people with well-established subject matter areas of expertise, and part of the reorganization would be to work toward balancing the workloads associated with the different portfolios as they are distributed across the branches. There may be some changes, she noted, but they would be well-advertised and the final structures would be brought back to Council.

Dr. Maddox applauded the DERT portfolio analysis, particularly as it relates to being able to drill down into the 1000 grants. She recommended that as the baseline is established, it would confer the ability to measure later outcomes as changes occur. She suggested looking particularly at the R01s from the perspective of early-stage investigators, allowing a great profile of the various sub-projects and how they may have changed and the scientists in those areas. Dr. Collman agreed.

VI. Big Data Initiative: NIH and Biomedical "Big Data"

Senior Advisor Dr. Allen Dearry described two new NIH initiatives designed to help overcome roadblocks presented by biomedical big data. The first is the Big Data to Knowledge (BD2K) program, which is intended to enable the biomedical research enterprise to maximize the value of biomedical data. The second is called

InfrastructurePlus, which creates an adaptive environment at NIH to sustain world-class biomedical research. The initiatives are both to be led by trans-NIH Advisory Data Councils: a Scientific Data Council to be chaired by the Associate Director for Data Science (a position currently being recruited), and an Administrative Data Council chaired by the NIH CIO. The councils will report to the NIH Director through the NIH Steering Committee.

BD2K will have four programmatic areas:

- Facilitating Broad Use of Biomedical Big Data
- Developing and Disseminating Analysis Methods and Software for Biomedical Big Data
- Enhancing Training for Biomedical Big Data
- Establishing Centers of Excellence for Biomedical Big Data

The program will be funded by a shared investment from the NIH Common Fund and individual ICs, for a total of approximately $100 million per year for the initial 5-7 years. Thereafter, the intention is to devolve the program to the individual ICs.

NIEHS has established its own Office of Scientific Information Management, comprised of the NIEHS Library, an Informationist program, and a data science coordination activity. NIEHS will establish its own Scientific Data Council to develop and support policies, standards, and infrastructure for data harmonization and integration.

VII. Update on the EHS Core Centers Program: Proposed New Guidelines

Dr. Les Reinlib briefed Council on proposed new guidelines for the NIEHS EHS Core Centers (EHS CCs) Program.

He cited several reasons to consider guideline revisions:

- EHS CCs are a foundation for building new programs and further serving communities.
- The current program is mature, with significant costs.
- Fixed budgets are limiting.
    - They restrain opportunities for centers with larger membership.
    - They provide little incentive to grow NIEHS support.
    - Shrinking budgets restrict NIEHS, limiting expansion to other research institutions.

He noted that currently the EHS CCs are concentrated in the Northeast and Midwest regions, creating "research deserts" in other areas and leaving many target communities underserved.

The proposal to revise EHS CC guidelines is in three parts:

- A sliding scale for competitive bids, linked to the sum of NIEHS-supported R01-type research
- Partner Awards – competitive awards to encourage collaboration with new teams, institutions and communities
- Opportunity Fund – administrative supplements to encourage resource sharing and cross-training

A term limit for CC directors is also proposed.

Dr. Reinlib emphasized that the proposals are not finalized and that comments and suggestions are quite welcome as the process moves forward.

Under the sliding scale, each center would still need to have 3 distinct PIs with at least one ES R01 and at least one year remaining on that grant. The budgets would be linked to the sum of the qualifying awards, applying to R01, R37, P01, P42, U01 and K grants. Every year a variable multiplier called an Index Figure would be announced in the RFA. The minimum requested budget should be $400,000 of direct costs, which could escalate $50,000 per year by demonstrating program growth. The maximum award would be $1.6 million in direct costs, which is roughly a $500,000 increase in the amount that is typically currently allowed.

It is projected that the new guidelines would save the institute somewhere between $1 million and $2.5 million per year under the worst-case, conservative scenarios. That is not to suggest that the program be cut by that amount, but that existing funds should be used in a more thoughtful, creative way, through new mechanisms such as the Partner Awards and the Opportunity Fund.

The sliding scale budgets would start with April 2015 funding at the earliest. The changes would only apply to competing renewals or new centers, and would not apply to non-competing centers. The proposed term limits on center directors involves a firmer transition plan, with two or three competitions for a director at a given institution, with a limit of 13-14 years for a director. This would encourage efforts to groom young investigators to move up into leadership positions.

Dr. Postlethwait asked whether there had been an attempt to model or extrapolate what the proposed revision of the core centers program might do to what has been "a zero-sum game for the last 25 years" in terms of adding new centers in the specified geographic areas. Dr. Reinlib replied that there is a bit of data, and the Institute does wish to see new centers established while recognizing that the existing center have done "a fabulous job over the years of supporting their investigators," and have grown the science in new ways that typical R01s could not have. He said that potential

applications tell him that they feel the program is very difficult to apply for, especially in times of flat budgets. He related that over the last seven years, there was a success rate with the existing center of almost 75%, while the success rate for new centers was only about 20%. He said there had also been a call from some of the existing directors to partner with other institutions, that being the concept of the Partner Awards, as a vehicle to bring new talent into the fold. He said that there were approximately 30 institutions with sufficient ES awards to apply, but that the NIEHS does not receive that many new applications. He noted that financial pressures would make things difficult, and that flat, across-the-board cuts had been one of the models considered.

Dr. Eaton endorsed the idea of term limits. He was concerned about the sliding scale approach in terms of what is or is not included. For example, he noted that NIEHS centers are very important elements of training programs, and excluding training programs would be a problem. Similarly, he was unsure about excluding P50 grants or U19 grants. He suggested that a simpler model might be just to look at the total NIEHS dollars at an institution, taking everything into account. With respect to the sliding scale, he was also concerned about the fact that NIEHS has research areas that cut across the boundaries of other institutes, and it seems paradoxical that some of that cross-cutting research might not be counted as EHS. This would have the effect of building siloes and inhibiting interdisciplinary work. While he was generally in favor of sliding scales, he said he was concerned that it could have the effect of basically eliminating the small centers, because many investigators would decide that it is not worth the effort to apply for $400,000 or $500,000 awards. Even at current levels, that has occurred, he noted.

Dr. Reinlib agreed that there would be a certain amount of uncertainty as to how the new guidelines would play out. He noted that there are a small number of core centers that exist at a lower annual budget. He said that over the past ten years there had been four centers with annual budgets of about $650,000 in direct costs. He felt that the ultimate question was whether there is a benefit to having a center regardless of how much money is involved. One answer is that centers end up leveraging other resources at their universities. He said there is likely to be a range of budgets. Dr. Eaton recommended raising the lower limit a bit to avoid eliminating smaller centers.

Dr. Gasiewicz said the Partner Awards were a great idea. He also expressed concerns about the sliding scale. He noted that R21 grants were not included, but should be. He said that counting grants from other institutes should also be considered, especially when NIEHS is listed as a secondary institute. This would allow leveraging of ES funds from other sources such as EPA or NIOSH. He made the point that CSR directs the destination of grant applications, and it could penalize investigators if their applications are directed elsewhere than NIEHS. He also noted that today it is difficult for any investigator to maintain a steady source of funding, with gaps sometimes occurring

when renewals come due. Thus, he suggested consideration of a rolling five-year average of ES funding, rather than basing decisions on a single time point. This would ensure that NIH is investing in institutions truly committed to EHS programs. He agreed that a budget of $400,000 would too often not be worth the effort involved, especially when it is so demanding to maintain state-of-the-art equipment and staff at core centers. He recommended that some blend of total NIEHS dollars and number of grants be considered; otherwise the grants may go disproportionately to centers that have only a few P01s or very large ES grants. He agreed with the rationale to attempt to save some dollars for the centers and devote them to areas where there are investigators clearly committed to EHS research. Thus, the institute needs to be careful not to designate center requirements that may actually impede rather than foster excellence in EHS research, regardless of the source of funding.

Dr. Boekelheide felt that the transition plan was a good idea. One element troubling him about the centers program was that it appears that "the rich get richer in this design," so that those who have big programs get more money. In some sense that seems fair, he said, but that is only true if those who get less money get it more easily. Noting the success rates cited by Dr. Reinlib, he said that discrepancy should be addressed within the new design.

Dr. Reinlib said that some of the questions broached led to the philosophical question, "What do you want the core centers program to do?" He noted that it does "a lot of good things just the way it is," so one option is to simply leave it alone. In some cases, the need for an ongoing center may be questionable. Otherwise, it is possible that at least some of the money could be used to build new programs and that seems like a compelling case to his group. He said that a plan such as the one proposed could both support existing centers and drive efforts to create new ones.

Dr. Hricko said she liked the Partner Awards idea a great deal, but that the focus on regional centers does not necessarily address the issue of the research deserts. She said she has concerns about the sliding scale in terms of the review process, and the COEC requirements as they might impact the smaller centers. She said she understood the thinking regarding term limits for directors, but felt that a hard rule might not be the best approach for that. Dr. Reinlib pointed out that NIEHS has been a leader in COEC activities and hoped that the amounts of money involved would be adequate for the smaller centers to perform reasonable outreach and engagement activities. However, some of the requirements may need to be re-thought at the lower funding levels.

Dr. Hu agreed that funding at $400,000 or $500,000 for a new center would not be worth the tremendous effort necessary to apply. He said he did not understand why the ceiling was to be raised to $1.6 million in a period of budgetary restraint. Regarding the

Partner Awards, he felt that there was an element of potentially partnering with one's future competition. He endorsed the Opportunity Fund concept, with a group being able to show how it could operate as a quasi-center without actually being a center, by running successful pilot projects and core facilities in collaboration with other centers.

Dr. Reinlib reiterated that it was difficult to anticipate how the proposed changes would play out, although he and his team have tried to model the scenarios. He said the program would be designed to give the institute some flexibility.

Dr. Gasiewicz commented that given the amount of time it takes even existing centers to put their applications together, the time frame to implement the proposed changes may be too tight. He recommended that if the changes are to be made, they should be made very soon to allow existing and new centers ample time to prepare their applications. Otherwise, he recommended delaying changes until they could be accommodated by existing Centers. Dr. Reinlib agreed with the point.

Dr. Eaton recommended that if the sliding scale is implemented, it should be based on direct costs, so as not to create an incentive by rewarding institutions with high indirect cost rates.

Dr. Birnbaum thanked Council members for their very constructive comments on the topic.

VIII. 2012 UNEP/WHO Report on the State of the Science of Endocrine Disrupting Chemicals (EDCs)

Dr. R. Thomas Zoeller from the University of Massachusetts Amherst briefed Council on the report issued by the United Nations Environment Programme (UNEP) and WHO, "State of the Science of Endocrine Disrupting Chemicals – 2012." Zoeller was a co-author and co-editor of the report, as was NIEHS Program Administrator Jerry Heindel.

The report updated the "Global Assessment of the State of the Science of Endocrine Disruptors" report, which had been issued in 2002. It consists of three chapters. The first chapter reviews the basic elements of endocrine disruption, written for a broad audience. It covers a targeted background in the field of endocrinology to lay the groundwork for understanding the challenges in identifying EDCs and determining whether exposures could produce adverse effects in human or wildlife populations. Chapter 2 reviews information largely published in the past decade focusing on links between chemical exposures and reproductive health, thyroid-related disorders, neurodevelopmental disorders, endocrine-related cancers, adrenal and metabolic disorders. The review clearly shows that the evidence supporting a role for chemical exposures in some human and wildlife disease has strengthened over the past ten years, but has weakened in others. Exposure science is the subject of the third chapter,

which shows that humans and wildlife are exposed to far more EDCs than just POPs ("persistent organic pollutants"), and that currently only a narrow spectrum of chemicals are even being evaluated in the environment. Emerging issues of concern are also covered in the third chapter.

Among the significant conclusions in the report was the concept that experimental studies are demonstrating very clearly the complexity of EDC actions on development and adult physiology, as new science emerges on delayed effects and epigenetic effects of EDC exposures. Zoeller noted that there has been a great deal of progress in the field in the past decade, and that NIEHS-funded research has played a very large role.

IX. Genome-Wide Interactions with Smoking – Served Two Ways

Intramural researcher Dr. Stephanie London described two recent research initiatives emerging from her laboratory using genome-wide analysis techniques to assess the impact of smoking.

The first program incorporated smoking into genome-wide interaction studies of pulmonary function in adults. London's group, along with collaborators, identified 16 novel loci that are responsible for determining proper lung function. It was a unique approach to genome-wide association studies (GWAS), expanding the method to yield previously unattainable results. The work showed that including environmental factors in GWAS using joint tests of main effects and interactions can discover novel loci that would be missed if genetic main effects alone were analyzed, with that being true even if the interactions are not strong.

The second section related findings from studies of epigenetic interactions with smoking, involving maternal smoking during pregnancy and genome-wide DNA methylation in newborns. Using a genome-wide methylation platform (the Illumina Methyl450K), London's group and collaborators from Duke University, the University of North Carolina at Chapel Hill and Norway found epigenetic effects suggesting that differing DNA methylation patterns in newborn children of smokers versus non-smokers may play a mechanistic role in adverse health outcomes later in the children's development. The work pointed toward two genes known to be associated with response to exposure to polyaromatic hydrocarbons contained in cigarette smoke, and to several other novel genes for smoking effects. The results support the hypothesis that epigenetic mechanisms may contribute to offspring health effects from maternal smoking in pregnancy. The studies also showed that the methylation differences seen for adult smoking in other studies are already present at birth in relation to *in utero* exposure.

X. Concept Clearance: Outstanding New Environmental Scientist (ONES) Program

Dr. Carol Shreffler presented the proposed renewal of the Outstanding New Environmental Health Scientist (ONES) award program, which seeks to identify and support the most talented early-stage EHS investigators.

The original ONES program was announced yearly for six years by a special Funding Opportunity Announcement, and between 2006 and 2012, 42 awards were made representing the spectrum of research areas supported by NIEHS. Those ONES grantees have been highly successful in their careers, and most have been retained in the field. The intention is to re-announce the program to make new ONES awards in 2015.

Council reviewers Drs. Gasiewicz and Cheung endorsed the concept. After discussion of issues such as budget flexibility and limiting the awards to one per school, Council voted unanimously in favor of the proposal.

XI. Concept Clearance: Environmental Contributors to Autism Spectrum Disorders (ASD)

Dr. Cindy Lawler briefed Council on the proposed new program announcement, "Environmental Contributors to Autism Spectrum Disorders." NIEHS has long had an extensive autism research portfolio, with investment in ASD research seeing significant growth, from zero dollars in 2002 to an estimated $8 million in 2012. The concept would continue and expand that support, while seeking to address gaps in research. The target is to release the PAR in January, 2014, with funding to commence in December, 2014. The PAR is to be active for three years, with a single receipt date each year.

Council reviewers Drs. Chesselet and Hu supported the concept. Council discussion included concern that the timeline from announcement to application may be too short. Council voted unanimously to approve the concept.

XII. Concept Clearance: Past, Present Future of Superfund Research Program R01 Mechanism

Dr. Heather Henry presented a concept for the next solicitation of the Superfund Research Program (SRP) R01. The SRP intends to develop a Funding Opportunity Announcement to explore the complex biological, geological and chemical processes that have implications for exposure risk by living systems. It is anticipated that 6-8 awards will be funding under the new announcement, which would continue the FY 2013 allocation of $1.5 million in funding. The RFA will be released in the fall of 2013, with the awards to be made in the summer of 2014.

Council reviewers Drs. Boekelheide and Kramer supported the concept. Council voted unanimously to approve the concept.

XIII. 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).

XIV. Adjournment

The meeting was officially adjourned at 12:00 pm on May 15, 2013.

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