

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

**MINUTES OF THE NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES
COUNCIL**

FEBRUARY 18–19, 2010

The National Advisory Environmental Health Sciences Council was convened for its one hundred twenty-ninth regular meeting on February 18, 2010 at 8:30 a.m. 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 18, 2010 from 8:30 a.m. to 5:00 p.m. and on February 19, 2010 from 8:30 a.m. to 9:30 a.m. In accordance with the provisions of Public Law 92–463 the meeting was closed to the public on February 19, 2010 from 10:30 a.m. to 12:00 p.m. for consideration of grant applications. Notice of the meeting was published in the *Federal Register*.

Members Present

Stephen Baylin, MD
Christopher Bradfield, PhD
Hillary Carpenter, PhD
David Christiani, PhD
John Essigmann, PhD
Rick Finnell, PhD

Stefani Hines, MA, MS
George Leikauf, PhD
Grace LeMasters, PhD
R. Stephen Lloyd, PhD
Sem Phan, MD, PhD
Jerald Schnoor, PhD
Kevin Stephens, MD, JD
Palmer Taylor, PhD

Ex Officio Officer

CPT Michael Macinski

NIEHS Staff

Kathy Ahlmark
Janice Allen, PhD
Beth Anderson
Bruce Androphy, Esq.
John Balbus, MD, MPH
Ralph (Eddy) Ball, PhD
David Balshaw, PhD
Linda Bass, PhD
Martha Barnes
Sharon Beard
Linda Birnbaum, PhD, DABT, ATS
Wanda Boggs
John Bucher, PhD
Jennifer Collins
Gwen Collman, PhD
Helena Davis
Caroline Dilworth, PhD
Christie Drew, PhD
Dorothy Duke

Sally Eckert-Tilotta, PhD
Benigno Encarnacion
Christine Flowers
Mary Gant
Barbara Gittelman
Kimberly Gray, PhD
Rachel Gross
Susan Hart
Astrid Haugen
Tom Hawkins
Jerry Heindel, PhD
Heather Henry, PhD
Michael Humble, PhD
Laurie Johnson
Paul Jung, MD, MPH
Edward Kang
Annette Kirshner, PhD
Stephen Kleeberger, PhD
Diane Klotz, PhD

Sandy Lang
Cindy Lawler, PhD
Stephanie London, MD, Dr. P.H.
Christopher Long
Liz Maul, PhD
Robin Mackar
Carolyn Mason
J. Patrick Mastin, PhD
Michelle Mayo
Kimberly McAllister, PhD
RoseAnne McGee
Elizabeth McNair
Srikanth Nadadur, PhD
Teresa Nesbitt, DVM, PhD
Sheila Newton, PhD
Aaron Nicholas
Heather Nicholas
Liam O'Fallon
Ted Outwater
Michelle Owens

Jerry Phelps
John Pritchard, PhD
Les Reinleib, PhD
Luci Roberts, PhD
Margarita Roque
Elizabeth Ruben
Barbara Shane, PhD
John Schelp
William Shrader, PhD
Carol Shreffler, PhD
Daniel Shaughnessy, PhD
William Suk, PhD
Claudia Thompson, PhD
Sally Tinkle, PhD
Michelle Victalino
Allen Wilcox, MD, PhD
James Williams
Mary Wolfe, PhD
Leroy Worth, PhD
Darryl Zeldin, MD

Members of the Public Present

Laura Bono, SafeMinds
Elizabeth O'Connell, Social & Scientific Systems, INC
Ken Portier, PhD, American Cancer Society
Jim Shannon, RTI International

OPEN PORTION OF THE MEETING

February 18, 2010 8:30 a.m. – 5:00 p.m.

I. CALL TO ORDER AND OPENING REMARKS

Dr. Linda Birnbaum called to order the one hundred twenty-ninth regular meeting of the National Advisory Environmental Health Sciences Council. She opened the meeting by welcoming those in attendance and informed everyone that, pursuant to the Governments in the Sunshine Act, all aspects of the meeting would be open to the public except for the review, discussion and evaluation of grant applications and related information. Dr. Birnbaum acknowledged Council members who were not present: Drs Graziano and Ramos and Ms Witherspoon.

She then invited everyone in the room to introduce themselves. Dr. Birnbaum pointed out that the open portion of the Council meeting was being webcast and instructed people to use their microphones when speaking.

II. REVIEW OF CONFIDENTIALITY AND CONFLICT OF INTEREST PROCEDURES

Dr. Collman reminded Council to sign conflict of interest forms, to speak into the microphones, and to state their name for the record when making comments.

III. CONSIDERATION OF MEETING MINUTES

A motion was made to approve the September 2009 minutes as written. The motion was seconded and approved unanimously by Council.

IV. REPORT OF THE DIRECTOR — Dr. Linda Birnbaum

Dr. Birnbaum opened her remarks by discussing the status of the FY 2010 appropriations and the President's Budget for FY 2011. She announced that the NIEHS budget increase in FY 2010 was the first time NIEHS received the highest percentage increase of all the institutes and centers at NIH. Congress recognized the translational research supported by NIEHS. The House encouraged NIEHS to support studies on the impact of endocrine disruptors. Concerns were expressed about the slow pace at which federal agencies have adopted regulations to replace or reduce animals used in testing. The Senate Report asked the National Toxicology Program (NTP) Center for the Evaluation of Alternative Toxicological Methods and the Interagency Coordinating Committee on the Validation of Alternative Methods to hold workshops on the challenges associated with the adoption of alternative methods.

President Obama's request for FY 2011 includes a 2.6% increase for NIEHS main appropriation and 3.2% for the Superfund Programs. The NIEHS amount is low because the budget for 2011 was generated in part using research areas categorized under the Research, Condition, and Disease Categorization (RCDC) classification system. These areas of interest for NIEHS were not adequately represented in the RCDC system, so our many of our research efforts were not captured. The RCDC system was not designed to be used as a budgeting tool, but the data is now being mined for budgetary purposes. Dr. Birnbaum indicated that we, along with other ICs, are working to align the RCDC terms with our interests.

Dr. Birnbaum described the status of various searches to fill open positions at NIEHS. Interviews for the new Scientific Director were delayed by the recent shutdown due to snow. The announcement for Director for the Division of Extramural Research and Training (DERT) closes at the end of month. The NIEHS Deputy Director solicitation closes in March. Dr. John Balbus has started as the Senior Advisor for Public Health in Bethesda. Dr. Aubrey Miller, currently at the Federal Drug Administration (FDA), has been named the Health and Human Services (HHS) liaison and will start at the end of March. We are still recruiting for a liaison to the toxicology community. She introduced Dr. Paul Jung as the new chief of staff. Mr. Bruce Androphy, J.D. is the new Ethics Supervisor. Recruitment is nearly complete for the education/outreach specialist; the top two candidates will be interviewed soon.

Several scientific advances produced by researchers in the Division of Intramural Research (DIR) were highlighted by Dr. Birnbaum. For example, an up and coming intramural investigator, Dr. Karen Adelman, uncovered a fundamental, evolutionarily conserved mechanism that controls TNF-alpha transcription in macrophages. She went on to highlight several papers published by extramural researchers supported by NIEHS. These included reports on mouse studies on effects of nanoparticle inhalation, the development of a high-throughput method to determine the methylation status of cytosine in a genome and to layer the resulting epigenomic map onto the genome it regulates, and a prospective study assessing the association between blood and bone lead.

Dr. Birnbaum went on to discuss several Institute honors and activities since last Council meeting. She was elected as a fellow to the Collegium Ramazzini, the international society of environmental health sciences and toxicology. She testified at two Congressional hearings

related to the Toxic Substances Control Act and will soon testify on endocrine disruptors in drinking water. Dr. Allen Wilcox received the 2009 Greg Alexander Award for maternal and child health. The Sisters Study, conducted by the Epidemiology Branch, has met its recruitment goal of 50,000. The Center for Evaluation of Risks to Human Reproduction convened an expert panel on the effects of infant soy formula. Strategic planning for the Superfund Research Program (SRP) is underway.

ACTION: Dr. Birnbaum indicated that results of the SRP strategic planning process will be available for September Council.

She described several activities pertaining to NIEHS interests in Global Climate Change. Several high-profile media events took place both in the US and abroad to emphasize the need to address potential human health effects of climate change.

On the outreach front, Dr. Birnbaum discussed the Worker Training Program's (WTP) speedy response in introducing its Earthquake Response Training Tool, made available online in Haitian Creole, for rescue workers in Haiti. Two Community Forums were conducted by NIEHS. One took place October 1 in Milwaukee, WI. The other was in conjunction with a grantee meeting with the Breast Cancer and the Environment Program, in Sausalito, CA on November 18.

Dr. Birnbaum updated the Council on scientific meetings attended or organized by NIEHS staff. The NIEHS booth at the American Public Health Association meeting in Philadelphia received first place. Grantee meetings were held in October for the NIEHS Centers for Neurodegenerative Science, and in January for the exposure biology program of the NIH Genes, Environment and Health Initiative.

Dr. Birnbaum closed her report by briefly touching on the research agenda of NIH Director, Dr. Frances Collins, which would be discussed further by Dr. Kleeberger later in the morning. She went on to update Council on the status of the NIH stem cell registry. She directed Council to the new Stem Cell Information page at <http://stemcells.nih.gov/>. She also informed Council that Dr. Bernard Kington will be leaving NIH this summer to take the position of President of Grinnell College.

Council Response and Discussion

Dr. Jerold Schnoor (Council Member) asked about climate change. EPA has decided to go forward with their plans to enforce greenhouse gas controls on power plants and automobiles. Are we helping EPA with that, in light of the public health impact and some of the controversy over the endangerment decision?

Dr. Birnbaum replied that NIEHS is working very closely with EPA. We led a cross-agency group in the development of a white paper on climate change. The publication of that white paper is delayed because of EPA concerns, but near completion.

V. LEGISLATIVE REPORT—Dr. Sheila Newton

Dr. Newton, Director of the Office of Policy, Planning, and Evaluation (OPPE), explained that the Legislative Report for Council had traditionally been part of the Director's Report, but because of Council's expressed desire to hear more detail in this area, a separate Legislative Report will be provided as needed. She reminded Council that Ms. Mary Gant is the NIEHS

Legislative Liaison and went on to summarize the various responsibilities under the OPPE. The OPPE assists on legislative language, pulls together information for testimony by NIEHS staff to Congressional hearings, coordinates information among NIEHS and NIH entities, and works with the financial management staff on appropriations materials.

She went on to recap recent Congressional hearings where NIEHS staff gave testimony. Dr. Newton indicated that 2009 was one of the most active years for NIEHS in terms of their participation in hearings. Dr. John Bucher, NTP Director, testified on September 15, 2009 on Health Effects of Cell Phone Use. In addition to the testimony described by Dr. Birnbaum in her report, she testified on the effects of the environment on children's health before a subcommittee of the Senate Committee on Environment and Public Works.

Current legislation of interest to NIEHS include HR 4160, Environmental Hormone Disruption Research Act of 2009; HR 4190, S 2828, Endocrine Disruption Prevention Act of 2009; and HR 4161, Women's Environmental Health and Disease Prevention Act of 2009. Dr. Newton described agency concerns with legislative language potentially creating an unfunded mandate or requiring the use of inappropriate funding mechanisms, and she indicated how her office works with congressional staff when possible to generate legislation that will serve the needs of both the agency and Congress.

Bills introduced recently focus on control and use of bisphenol-A (BPA). One bill, HR 4456, BPA-Free Kids Act of 2009, would require NIEHS to undertake a 5-year effort to increase understanding of health effects of BPA. It authorizes \$5M/year for FY2010-2014, although the funds are subject to appropriation by Congress.

In addition, a couple of bills have been introduced by members of the Senate Committee on Small Business and Entrepreneurship that would reinstate the SBIR set-aside in ARRA funds, a concern if passed because those funds are already spent.

Dr. Newton closed her report by describing the process of what happens after a bill is passed by Congress. She used the Breast Cancer and the Environment Act of 2008 as an example. She also provided several sources where Council could obtain information on pending legislation and hearing testimony.

Council Response and Discussion

Dr. John Essigmann (Council Member) thanked Dr. Newton for her report and indicated that he hadn't realized the short timeframe under which she worked. He asked if Dr. Newton could brainstorm how the extramural community could help her come up with the strongest cases for legislation that would serve the environmental health community.

Dr. Newton replied that deadlines are often short, and we generally rely on our database sources for quick, comprehensive data about the NIEHS research portfolio.

Dr. Birnbaum went on to describe how testimony is prepared, often within a very short time frame. Every statement has to be referenced and 100 copies of the documentation must be sent to the committee. All statements have to be cleared by several people. Then the oral testimony must be prepared, condensing it down to 5 minutes. The response to questions is challenging because you don't know what they will ask. Sometimes questions are off-topic, and written questions can appear up to 2 weeks after the testimony.

Dr. Newton followed up with an explanation that the appropriation process is completely different from the hearing testimony. She works with the budget office over an extended period of time on materials to support the NIH director in his justification for budget requests.

Dr. Jerold Schnoor referred to Dr. Birnbaum's comment in her report about the lower proposed budget for NIEHS in FY 2011, and asked about news coverage that NIEHS receives about its activities. Has NIEHS benchmarked against other institutes, and how are we doing? He also mentioned the NIEHS journal, Environmental Health Perspectives (EHP), as a way to get our news out to Congress and into the community.

Dr. Birnbaum explained that news coverage is tracked by Ms Christine Flowers in the Office of Communications. She indicated that NIEHS coverage is comparable to that of other institutes. With respect to EHP, she frequently writes editorials and policy papers.

ACTION: Dr. Birnbaum went on to say that Christine Flowers could provide a report next Council.

VI. RETREAT REPORT—Dr. Steve Kleeberger

Dr. Kleeberger began his report by thanking Drs. Collman and Newman for organizing the retreat. He thought it was productive and fun.

ACTION: Dr. Kleeberger went on to say that he would give a more complete report on the retreat at a later Council meeting.

Dr. Kleeberger indicated that the intent of the retreat was to focus on NIEHS's priorities that fall under Dr. Collins' research agenda as described recently in the journal Science. After briefly listing the items in Dr. Collins's list, Dr. Kleeberger said he decided to focus his report on identifying NIEHS activities consistent with opportunities under Dr. Collins' agenda, and thinking creatively about addressing those opportunities. The salient points that came out of discussion are as follows:

High-throughput Technologies (HTTs): many opportunities exist for environmental health sciences (EHS) in this area. Examples include using HTTs to understand dose response and approximate systems response and for developing a chemical atlas. Better information is needed on how to move forward in training biostatisticians. How can individual investigators use available HTTs and datasets? The funding pipeline must be balanced between creating resources (mice, cells) and validating translation into practice.

Translating basic science into new and better treatments and outcomes: understanding environmentally mediated pathogenesis and risk of disease can lead to treatments, including screening that incorporates genetic and other susceptibilities. With regards to outcomes, research is needed leading to interventions at multiple levels. Studies to compare effectiveness of approaches are needed. Focus should be shifted to early exposures not just late disease. Prevention should be stabilized as an NIH goal. Translating environmental interventions is a political process, not examined from a comparative medicine standpoint.

Reinvigorate biomedical research: overlap include the pipeline of young investigators and recruitment and retention of minority scientists. Methods for foster innovations are needed, resulting in structures that support creative chaos, improvisation, and high-risk research within a guiding structure. A new innovative P01 program was suggested. Kudos should be given to the extramural program ViCTER, Virtual Centers for Transdisciplinary Environmental Research.

Health care reform: opportunities include comparative effectiveness research of prevention versus other strategies; risk factors for disease, prevention strategies and personalized medicine; understanding correlations between genotype, drug genotype and environmental exposure; health disparities research; and health economics research.

Global health: domestic health is not separate from global health, and training and education go together with global health. A military and defense dimension exists. Our focus is on primary versus secondary prevention. There is a challenge of balancing emerging versus ongoing global health, i.e., oceans. We must be concerned with selling EHS with global health.

Dr. Kleeberger then asked for questions.

Council Response and Discussion

Dr. Grace LeMasters (Council Member) asked if the Oceans and Human Health Center Program, previously offered in the extramural grant program, had ended.

Dr. Birnbaum replied that the former iteration of the program is ending, but a new, reinvigorated announcement will be published in FY 2011.

Dr. LeMasters asked if the new program would be focused on oceans, rivers, or other water sources. She mentioned that river water is a common source of drinking water and has great impact on human health.

Dr. Birnbaum agreed that research results have demonstrated the importance of rivers. She went on to say that various initiatives are being looked at for the solicitation and to stay tuned.

Dr. Stephen Baylin (Council Member) asked if the HTT focus would be on cell-based technologies. He stated that many technologies are relevant to risk assessment and prevention, but cell-based technologies may not be the most relevant.

Dr. John Bucher, NTP Director, indicated that while they realize that they are looking at immediate readouts with the cell-based assays, they believe the readouts are relevant to long-term outcomes.

Dr. Baylin inserted that one would need to know the steps involved to relate immediate responses to the long term.

Dr. Bucher replied that they are bringing in pathways to understand the links with disease.

ACTION: Dr. Birnbaum inserted that a presentation on Tox21 would be good to have in either the May or September Council meeting.

Ms Stefani Hines (Council Member) observed that the recent Council retreat was different from those in the past. She thought that having everyone in the conversation resulted in a richer discussion. She thanked NIEHS staff for the opportunity.

Dr. Kleeberger expressed enthusiasm for the outcomes of the retreat. Council broke for 15 minutes before the next report.

VII. REPORT, CHAIR, BOARD OF SCIENTIFIC COUNSELORS FOR NTP—Drs. John Bucher and Ken Portier

Dr. Bucher introduced Dr. Ken Portier, Chair of the Board of Scientific Counselors (BSC) for NTP, and provided context for Dr. Portier's report. He went on to describe the policy and scientific oversight structures for NTP.

Dr. Portier described the BSC composition, its charter and responsibilities. The BSC reviews the contract concepts for research activities and literature analyses. He reported on 22 studies for testing nominations and 8 research studies using multiple mouse strains to assess the roles of genetics to toxicity. The BSC provided input on literature analysis activities by the Center for the Evaluation of Risks to Human Reproduction. The Board routinely advises NTP on criteria to evaluate findings and makes recommendations. They conduct peer review on draft reports containing policy decisions, draft NTP technical reports and briefs, and draft substance profiles.

He then asked Council for any questions they may have.

Council Response and Discussion

Dr. Palmer Taylor (Council Member) asked how much impact the BSC has downstream with policy makers and regulatory agencies.

Dr. Portier responded that the BSC has members from FDA, and as a result, recommendations go directly to the FDA with considerable weight.

Drs. Birnbaum listed several other instances of cooperation between NTP and FDA. She indicated the FDA is a key partner, and peer-review research results have a great deal of impact on FDA actions. Dr. Bucher indicated that they are very helpful when NTP seeks to interact with commercial entities.

Dr. Portier referred to Dr. Kleeberger's previous report on the retreat and added that NIEHS has been a consistent supporter of training in biostatistics. He would strongly encourage continuing that emphasis.

VIII. SCIENCE SEMINAR, GENETIC SUSCEPTIBILITY AS A CAUSAL TOOL IN ENVIRONMENTAL EPIDEMIOLOGY—Dr. Allen Wilcox

Dr. John Pritchard introduced Dr. Wilcox, who is the head of the Reproductive Epidemiology Group in the Epidemiology Branch at NIEHS.

Dr. Wilcox began his talk by discussing the need for tools to determine when a factor is causal for a disease or disorder. Genetic susceptibility is such an etiological tool, and he proceeded to demonstrate its use by focusing on a case-control study of the environmental causes of facial clefts.

In collaboration with a group in Norway, NIEHS gathered a wealth of genomic data on mother/child pairs where the child was born with and without facial clefts. Researchers expect to find genetic influences that would explain the high familial risk, but such genes probably account for a minority of the facial clefts. As a result, environmental exposures are an important influence. The study proposed to find exposures associated with clefts, identify genes playing a role, and assay both maternal and fetal genotypes. One gene at a time would be considered, chosen by biological plausibility, consistency, and coherence. They would then replicate positive associations.

The study looked at smoking, maternal folic acid supplements, and maternal alcohol binge drinking during the first 3 months of pregnancy. While a two-fold relative risk of fetal clefts was found with maternal smoking, no evidence of genetic susceptibility was found. For folic acid supplements, researchers found one gene associated with metabolism of folic acid that seemed to have an effect, but it was in the wrong direction. No plausible evidence was found for genetic susceptibility, despite expanding the search for other genes.

Maternal binge drinking showed a relative risk of 2.2–2.6 for 5+ drinks per sitting. Data showed that if the child had no risk allele, then there was no cleft. If a risk allele was present, but no maternal alcohol, then no cleft. However, there was an increased risk of cleft if both risk allele and alcohol were present. The link is biologically plausible, but the study has not yet been replicated.

Genetic susceptibility is challenging because there are so many choices: genes, SNPs, haplotypes, potential multiple genes, gene-gene interactions, and epigenetic mechanisms. Many false positives can be generated.

Dr. Wilcox concluded his talk by stating that expectations for the use of genetic susceptibility have been too high, false positives were underestimated, replication is difficult, and the biology is complicated. However, promising new tools exist, such as genome-wide interaction studies (GWIS).

Council Response and Discussion

Council members had several questions on the contributions from specific genes to facial clefts, as well as methods for sorting out maternal and fetal alleles. They and Dr. Wilcox discussed the difficulties in dealing with a unique cohort which is underpowered. Several suggestions were made regarding animal studies which could be explored and other cohorts in populations that may provide additional information.

Council broke for lunch.

IX. REPORT OF THE INTERIM DIRECTOR, DERT—Dr. Gwen Collman

Dr. Collman began her report discussing the budget updates and activities for FY2009. She demonstrated the distribution of grant funding among mechanisms and by activity. Dr. Collman pointed out that two Pioneer awards were given to NIEHS grantees. Pioneer awards are given by the NIH Office of the Director (OD) in recognition of cutting-edge research with potential for forwarding science in their respective areas. She listed the raise-to-pay and bridge (R56) awards given in FY2009 and explained the use of the R56 funding mechanism. In discussing the NIEHS success rate, Dr. Collman stated that it is not as good as that of the overall NIH, but has been fairly stable over the past few years at around 18–20%. NIEHS is around the middle when benchmarked with other institutes, better than the bottom as in previous years.

Moving on to the ARRA (Stimulus funds) funding, Dr. Collman discussed the OD's solicitations and co-funding. One particular program, supporting sustainable community-linked infrastructure, is particularly good for non-academic partnerships. NIEHS is thinking about \$5 million commitment in this area. We are also planning some supplements for summer students under ARRA.

Targets have been listed for benchmarking support for new investigators against other institutes. NIH uses these for targets only and there is no specific number required. ARRA provided an additional way to exceed our goals in this area. The ONES program has been a key program to meet these targets because we get a number of high-quality applicants. By putting out targeted solicitations, we have been increasing the number funded over time.

The Loan Repayment Program for FY 09 received 27 applications and awarded 20 (11 clinical, 9 pediatric). This year, 25 applications have been received, and decisions will be made in August.

Dr. Collman went on to discuss the accomplishments of the Breast Cancer and the Environment Centers (BCERC) working group. The group is key for improving communication between the working group, agency staff, investigators, and community outreach members. Among other accomplishments, it has facilitated and broadened trans-disciplinary efforts as the program has transitioned to a network.

Various staff activities were highlighted by Dr. Collman. Among them were activities at the meeting of the International Society of Exposure Science Nov 1-5, 2009. Dr. Caroline Dilworth chaired a symposium session supporting community-level exposure assessment. The Genes, Environment and Health Initiative, Exposure Biology Program staff led a session to assist in forging collaboration between epidemiologists and technology developers. At the American Public Health Association November meeting, Dr. Collman was a panelist on the coordination of federal partners and Liam O'Fallon represented the Partnerships for Environmental Public Health Program. Dr. Collman and staff from the Worker Training Program (WTP) participated in a conference on Environmental Justice (EJ), Air Quality, Goods Movement, and Green Jobs in New Orleans. This conference focused on high-level discussion with EPA for incorporating EJ components into their regulatory jobs.

Dr. Collman mentioned several workshops which will take place in the next few months before going on to talk about the latest developments with Enhancing Peer Review. She discussed the shortening of applications and emphasized the change in correction window for applications to ensure their compliance.

Dr. Collman explained how the early concurrence program works since changes in scoring system. Grant applications are included if they are at or below 10th percentile or priority score 27, with direct cost below \$500,000, and with no bars or concerns. All R13 conference applications go to early concurrence.

Council action was required on consideration of delegated authorities. Dr. Collman specifically talked about #11 which raised the threshold on awarding supplements without Council concurrence, instigated last year because of ARRA. She would like to keep this clause in delegated authorities since ARRA funds are still being awarded. The other two areas for approval are #5 and #9 which update language to reflect current NIH policies or language.

A motion was made by Dr. George Leikauf to accept the named changes to the delegated authorities and approved unanimously by Council.

Council Response and Discussion

Dr. Palmer Taylor asked for clarification on Item #11 on the delegated authorities. Dr. Collman explained the difference between ARRA supplements and regular grant mechanisms.

Dr. Taylor referred to the NIEHS success rate and asked if it were to be ranked relative to R01s, how does NIEHS compare to other institutes?

Dr. Collman replied that NIEHS is relatively similar to other institutes.

Dr. George Leikauf referred to the slide on awards for RPGs. He observed that the total amount is less than 50% of the total NIEHS budget. He wanted to know how that compares with other institutes. How will spending increase with the budget increase for FY2010? He stated that he would like to see at least 50% of money received by NIEHS to go to research grants.

Dr. Birnbaum stated that she saw his concern, but pointed out that NIEHS is unique in several ways. It has a fairly large intramural program, relative to other institutes, and, in addition, it is home to the NTP. She also pointed out that numbers listed don't include roughly \$152 million in extramural R&D contracts.

ACTION: Dr. Birnbaum said that while she does not have expenditure figures for other institutes, she could get them.

Dr. Leikauf indicated that contracts are initiated internally, not from extramural scientists. While the NIEHS payline is fantastic, he doesn't like the graph that shows NIEHS is at the low end with regards to extramural funding.

Dr. Birnbaum responded that we hear that you want more grants to be funded. Our money comes in different pots and we have very limited flexibility to move funds from one pot to another. In addition to grant programs, we have programs that rely heavily on contracts and in-house programs, including basic personnel costs. Contracts go through a competitive review process.

Dr. Collman pointed out that most of the FY2010 increased funding has been designated by Congress as to how it can be used.

Dr. Leikauf stated that it should be a long-term goal to increase the NIEHS payline up to that of the overall NIH.

Ms Stefani Hines observed that it is difficult to look for Council to look at a bottom line number without understanding the complexity of the budget. Council needs to have a better understanding of the complexities of the bigger picture. She thought this was an area where there can be rich conversation between Council and staff.

ACTION: Dr. Birnbaum said that we will schedule a better briefing on the budget processes and constraints in May or September Council meetings. Laurie Johnson will coordinate this activity.

Dr. John Essigmann asked if it is getting near the time when NIH will reassess trainee stipends.

Dr. Carol Schreffler (NIEHS DERT Training Program) explained that the training officer at NIH looks at stipend levels, and petitions Congress for increased funds for stipends. Otherwise, it is a trade-off between stipend levels and number of slots. NIGMS has the majority of pre-doctoral slots and takes the lead on these recommendations.

Dr. Palmer Taylor asked if authorization is needed to move funds out of research and into training, and Dr. Schreffler indicated that it is.

Dr. Collman announced that council members will be asked to respond to a survey on enhanced peer review after adjournment.

Dr. Birnbaum thanked Council for all the action items.

X. SCIENCE SEMINAR, GENOME-WIDE ASSOCIATION STUDIES OF ASTHMA AND PULMONARY FUNCTION—Dr. Stephanie London

Dr. John Pritchard introduced Dr. Stephanie London, who is head of the Genetics, Environment and Respiratory Disease Group within the Epidemiology Branch.

Dr. London focused her talk on the genome-wide association studies (GWAS) she has participated in to study childhood asthma and adult pulmonary function. She described approaches typically used before the initiation of GWAS, positional cloning and candidate gene association, and listed the disadvantages of each. She stated that GWAS has gained in popularity as the available technology has improved. GWAS is very good at finding associations between genes and a disease, but it's not so useful for determining causal relationships.

Childhood asthma etiology is still not well-defined, despite how long scientists have been studying the disease. Dr. London described the risk factors, e.g., being from a developing country, being allergic, and having a family history of asthma. We know that there are environmental triggers for symptoms, but the etiology of environmental risk factors is less clear. The pre-GWAS genetic picture was also poorly delineated. Associations had been discovered, but replication was spotty and no genes had been firmly established to influence asthma risk.

Dr. London discussed two GWAS studies on asthma, Moffat, et al. in 2007 and Weise et al., before moving on to the Mexico City study NIEHS conducted. The Mexico City Childhood Asthma Study found several low p-value genes, and the researchers then attempted to replicate the resulting correlations. Correlations in two small p-value SNPs were statistically significant. These are biologically plausible for asthma risk from animal and other models. Dr. London went on to talk about the ancestral study that was then conducted. They are currently participating in a meta-analysis with other asthma GWAS studies.

She then spoke on their GWAS study on adult pulmonary function. She described pulmonary function measurement and factors that influence function in adults. Due to the small number of samples Dr. London and her colleagues had available, the researchers engaged with several consortia to accumulate enough subjects to power their GWAS studies. A number of findings were found, some confirmed previous studies, and others suggested additional associations.

Dr. London closed her talk with future directions of her work.

Council Response and Discussion

Dr. Stephen Baylin asked Dr. London about the potential mouse models she would be using.

Dr. London replied that she will need to work with someone with understanding of the various mouse models.

Dr. Birnbaum asked if it was too simplistic to try to identify causal genes.

Dr. London responded that some of the complex layers look at gene-gene interactions. The CHARGE analysis will have the power to look at pathways, but it is in the computational phase of trying to look at pathways.

Further discussion took place between Dr. Sem Phan (Council Member) and Dr. London on the stratification of the population.

Dr. Birnbaum thanked Dr. London for her seminar and called for a break before the next talk.

XI. SCIENCE SEMINAR, USING SIBLING PAIRS TO STUDY THE EPIGENETIC EFFECTS OF PRENATAL PAH EXPOSURE— Dr. Julie Herbstman

Dr. Collman introduced Dr. Julie Herbstman, who is an extramural scientist and NIEHS grantee from Columbia University.

Dr. Herbstman described her interests in the effects of early exposure to polycyclic aromatic hydrocarbons (PAHs) and her efforts to use sibling pairs to study the epigenetic effect of that exposure. She focused her talk on studies on DNA methylation, important because it's involved with transcription.

She described the factors that affect methylation of DNA, and went on to describe sources of PAH exposure. She stated that evidence exists linking pre-natal exposure of PAHs with adverse health outcomes. It's important to delineate the underlying mechanism to identify methods of prevention.

Evidence supports the hypothesis that PAHs affect DNA methylation. Dr. Herbstman emphasized the importance of the pre-natal critical window when fetal exposure could affect methylation which can persist into adulthood. She described the cohort of mother/child pairs and the sub-sample taken for her studies. Her studies found that pre-natal exposure was associated with global hypomethylation in cord blood. Blood from follow-up studies showed about the same measure at 3 years, demonstrating that global methylation level persists from birth to 3 years.

Dr. Herbstman went on to ask if pre-natal exposure to PAH is shown to be associated with methylation of specific genes and which genes would be appropriate to look at. Preliminary studies have not shown a difference in methylation with and without PAH exposure for several genes they have looked at. In an effort to delineate differential effects from exposure to PAHs, additional studies are underway using a sibling-pair approach.

Council Response and Discussion

Dr. Stephen Baylin stated that loss of methylation in PAH exposure can indicate risk to cancer, so he advised that she not ignore outlier data.

Dr. Birnbaum pointed out that control of gene expression is more associated with non-CpG sites, but that their study is not looking at those sites. She also stated that cord blood only shows current exposure and not that of the critical developmental window.

Dr. Herbstman responded that some validation studies have been done to see if short measurements of PAH exposure are representative of gestational exposure. There are some

other measures we can use, such as metabolites in urine. She agreed that the critical window is important.

Dr. Kevin Stephens (Council Member) asked if she had looked at birth endpoints.

Dr. Herbstman said that they need to understand the construct first, before starting to apply it.

Dr. Fred Tyson (NIEHS) asked if she had looked at any imprinted genes, and Dr. Herbstman agreed that was a good place to look.

Dr. John Essigmann asked if there were animal models that could be run concurrently. He also asked if there were studies looking at the epigenomes of the kids.

Dr. Herbstman described studies where they are looking at target tissue in mice, but she didn't know if the epigenomes of the kids were being studied.

XII. COUNCIL DISCUSSION OF ISSUES

Dr. Collman announced that there were 30 minutes to cover issues that Council would like to bring up.

Dr. George Leikauf brought up thoughts on innovation from the Council retreat. He suggested looking at the R21 portfolio to quantitate innovation. NIEHS could get a panel together to come up with criteria for innovation using objective and subjective measures, and divide the applications into piles based on their view of innovation. Then adjust the portfolio if the pile of innovative grants is not large enough. NIEHS should not try to address innovation without determining criteria and looking at it in a systematic way.

ACTION: Dr. Birnbaum stated we should look to find a way to figure out a metric for innovation.

Dr. Grace Lemasters pointed out that applications are judged by innovation in peer review.

Dr. George Leikauf responded that study sections are conservative and innovation is being reviewed out.

Dr. Essigmann thought that certain words could be mined from pink sheets to come up with words that correlate with innovative outcomes.

Dr. Birnbaum asked if new and innovative were the same? New is not necessarily risky. If you want to be innovative, you have to go away from likely to succeed.

Dr. Lemasters suggested finding out which sections were most predictive of funding, put that data into a model to predict funding.

Dr. Collman remarked that NIEHS could look at how we make funding decisions. She pointed out the component scores, which could be used in decision-making rather than using the overall priority score.

Dr. Christie Drew (NIEHS) stated that RCDC had a difficult time identifying high-risk, high-reward science. We would need metrics to define innovation.

Dr. George Leikauf thought a panel of scientists looking at R21s could make this determination. What was new four years ago is not new today.

Dr. Collman pointed out that R21s are not necessarily high risk; some institutes don't always use them that way.

Dr. Jerold Schnoor remarked that innovation and high risk are all subjective, so we will need to be very specific. A definition might be novel with high probability of success.

Dr. Birnbaum suggested that was one definition, but the DARPA definition, for example requires an idea to be outside the box. If it works, fine, but if it doesn't, then it was worth the chance.

Dr. Collman responded that one in a thousand R21 will have that profile, while the rest are getting more preliminary data to support an R01.

Dr. Essigmann asked if NIH can look back 50 years and examine the outcomes to see what characteristics there are in an application that indicated an innovative ideas that later became successful. Dr. Baylin thought it was done but it was hard to find any particular thing in anyone's grant application.

Dr. Taylor pointed out that Pioneer grants and new investigator are different, one takes a flyer at an innovative idea, where new investigators put everything they have in that idea. It's difficult to evaluate innovation over short periods of time because outcome from research takes so long.

Dr. Collman suggested that NIEHS could follow challenge grants, because they are focused on innovation and a set cohort. You could look at the way the applicants framed their questions that made the reviewers think they were innovative.

Dr. Leikauf asked if the success of the ARRA program will be evaluated?

Dr. Collman responded that everyone would like to know what we got out of ARRA. We have set up our system to gather data to measure success. She went on to say we can target programs with specific communities/grantees with specific goals. Superfund and WETP had specific goals in their programs. Traditional supplements would be difficult. Dr. Birnbaum pointed out that the Grand Opportunity grants have to demonstrate what has come out of them.

Dr. Leikauf stated that Congress will want to know the bottom line and what we got out of ARRA to determine mandates.

Dr. Drew pointed out reports on NIH webpages that talk about ARRA funds investment.

Dr. Birnbaum thanked Council for the discussion and adjourned for the day at 4:30 pm.

EXECUTIVE CLOSED SESSION FOR COUNCIL

XIII. OER SURVEY TO COUNCIL ON PEER REVIEW ENHANCEMENT

Dr. Collman introduced Luci Roberts, Health Science Policy Analyst, from the Office of Extramural Research, NIH, who discussed the mandate that the Enhancing Peer Review process must engage in evaluations to facilitate improvements in the process. She described the survey plans and indicated the intent was to determine how enhanced peer review has affected Council's ability to do their jobs. In response to questions from Council Members, she

said that the survey on that day will be baseline. She asked that Council exclude ARRA and recent changes, such as the shortening of applications. She asked that Council members only respond within that role and not as a grantee.

OPEN PORTION OF THE MEETING

FEBRUARY 19, 2010 8:30 – 9:20 am

XIV. DISCUSSION OF EVALUATION PLAN FOR P30S AND FUTURE OF THE P30 PROGRAM—Drs Les Reinlib and Christie Drew

Dr. Reinlib reminded Council that they were in open session, and that discussions on specific applications in the Core Center Program must wait until closed session. He then talked about the goals of the Core Center program, it: supports centralized facilities for funded investigators; stimulates multidisciplinary approach; supports translation by implementing outreach and education; provides access to cutting edge instrumentation; and promotes leadership in EHS.

Changes in guidelines were initiated in 2007 to cut program costs and enhance collaborations and phased in over four years. Community Outreach and Education Cores (COEC) became optional, although this decision was reversed for FY11, and changes were made to allow for more flexibility in the budget. There were 25 centers in 2006, and there are 19 centers in 2010. NIEHS is nearing the goal set by the previous Director of cutting program by one-third.

Dr. Drew spoke on the upcoming assessment of the P30 program. She emphasized that this was an interim assessment, and a larger, in-depth evaluation would likely take place in a later time frame, e.g. 2014-15. The goals of the assessment are to understand changes that have taken place and inform the 2012 funding opportunity announcement.

She said that she is currently assembling the internal team and will recruit two Council Liaisons to participate. The assessment will be conducted in house throughout the spring and summer. Liaisons will participate in a series of meetings to finalize assessment questions, collect and analyze data, and develop conclusions and recommend changes to the announcement. Topics to be addressed include the following: the integrated health sciences facility cores; the director's fund, pilot projects; the COEC community advisory boards; career development and new investigators; and changes to the scientific review scoring system.. Primary and secondary data sources will be used. The timeline is very fast, to inform the next solicitation.

[Editors note: Two members, Dr Stephen Lloyd and Dr. Palmer Taylor, have subsequently volunteered to be Council Liaisons].

Council Response and Discussion

Dr. Collman explained that this discussion was brought before Council because it has expressed a desire to talk about the P30s in the past. The 2006 evaluation provides a benchmark to use in comparisons.

ACTIONS: Council Members are requested to email any additional questions or concerns.

Dr. John Essigmann referred to the slide showing a map of centers across the US and asked if NIEHS will look at what has been lost and use that as guideline for any further cuts to the program?

Dr. Reinlib responded that we have discussed it and want to know. The map shows a large geographical area with no P30 centers. We also want to know how well a center serves the community it is in. What has it done?

Dr. Stephen Lloyd referred to the facility cores and asked if centers can show how much of their budget is supported by the grant. Are they highly leveraged? This should be included in the evaluation.

Dr. Reinlib said that we know that when a center is lost, facilities are not being supported.

Dr. David Christiani stated that there are loaded assumptions on assessing contributions of a center to the community, and he wouldn't be too concerned if there are no centers in the middle of the US. What happens when areas don't have the infrastructure to support a center? It's possible to dilute the effort by trying to get centers in low population states where there isn't a critical mass of researchers and expertise.

Ms. Stefani Hines named some metrics that could be used. A retrospective look is good. NIEHS could interview previous center directors. Translation may need to have a broad definition. She suggested that the assessment should look at number of applications submitted not just at funded applications.

Dr. Palmer Taylor asked if there would be site visits. He also pointed out that looking back, you'll see centers serving other institutes and the broader community. There is an economy of scale.

Dr. Drew responded that site visits are beyond the scope of an assessment of 6 months.

Dr. Essigmann pointed out that there used to be a standing subcommittee of council for P30s; it might be good idea to reconstitute it so center directors see that discussion. He stated that he would like to have the opportunity, since the program is high impact.

Dr. Collman explained the purpose of the subcommittee was not for outreach but to have informed reviewers.

Dr. George Leikauf said there used to be career investigators in the Core Centers to support big science, but it's not true anymore because of the reduced funding. Over the years, how many dollars are going to support staff in the centers? They could provide stability that isn't there now.

Dr. Birnbaum thought there needs to be a look at the extramural portfolio to see if we are supporting what we need. The distribution of grant mechanisms may not be appropriate. Talking about the P30 program in isolation will not get us where we want to be.

Dr. Kevin Stephens brought up the potential for sun setting programs to ensure innovation. After a long time of funding, grants may seem to be an entitlement.

Dr. Collman said the previous evaluation should be circulated as background (**ACTION**). We have had specific RFA's to bring in new centers, i.e., P20s.

Dr. Stephens said he liked the concept of “birthing centers.”

Dr. Stephen Lloyd asked if NIEHS discourages applications from universities not associated with a medical school? Is the lack of an affiliated medical school adversely affecting new applications?

Dr. Collman responded that it's a real issue and has been discussed with center directors. NIEHS puts out broad guidelines and tries to assist in the development of new applications. In the last iteration, we added flexibility, and we will see if flexibility was successful.

Dr. Birnbaum thanked the Council for discussion, and stated that it was necessary to move into closed session to ensure that Council completes its work before members had to leave.

CLOSED PORTION OF THE MEETING

FEBRUARY 19, 2010, 9:30 - 12:00 pm

Dr. Collman reminded Council members of their obligations under conflict of interest regulations.

XV. CONSIDERATION OF GRANT APPLICATIONS

This portion of the meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the FACA, as amended (5 U.S.C. Appendix 2).

The regulations concerning conflict of interest were reviewed. Council members were reminded that materials furnished for review purposes and discussion during the closed portions of the meeting are considered privileged information. All Council members present signed a statement certifying that they did not participate in the discussion of, or vote on, an application from any organization, institution, or any part of a university system, of which they are an employee, consultant, officer, director or trustee, or in which they have a financial interest. Institutions or organizations which have multi-campus institution waivers, or are specifically designated as separate organizations under 18 U.S.C. 208(a), are exempt from this provision.

The February 2010 Council considered 331 NIEHS applications requesting \$140,147,310 in total cost and recommended 196 applications with a total cost of \$97,460,017.

Council voted and unanimously concurred with the review of applications under the EN Block action and the ARRA program. Several applications within the grey zone were discussed.

Mr. Ted Outwater (NIEHS) presented the program plan for the WETP SBIR Program for RFA ES09-006 E-learning for HAZMAT and Emergency Response. Council voted and unanimously concurred with the review of the applications under that solicitation.

Dr. Jerold Heindel (NIEHS) gave an informational report for institutional training grants. During discussion, Council members suggested a reconsideration of the timing for solicitations for training grants, as the present timeline is difficult for researchers to recruit students.

Dr. Bill Suk (NIEHS) asked Council to approve a 1-year extension with cost to a cooperative agreement with WHO to allow time to deal with leadership changes. Council voted and unanimously approved the request.

Before Drs Birnbaum, Collman, Kleeberger, and several Council members recused themselves for conflicts of interest, Council members expressed their gratitude to Dr. Birnbaum for her leadership since taking the director position. She has accomplished a great deal, and the openness in which she has done her job has been appreciated.

Dr. Pat Mastin, Acting Deputy Director of DERT, presided over Council in Dr. Birnbaum's absence. Dr. Heather Henry (NIEHS) presented the program plan for the Superfund Research Program P42 solicitation. After discussion, Council voted and unanimously concurred with the review of the applications.

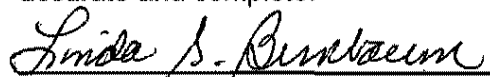
Dr. Les Reinleib presented the program plan for the P30 Core Center Program solicitation. Council voted and unanimously concurred with the review of the applications.

XVI. ADJOURNMENT OF THE NAEHS COUNCIL

The meeting was adjourned at 12:00 PM on February 19, 2010.

CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.



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



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

Attachment:
Council Roster