

**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**

May 30-31, 2007

The National Advisory Environmental Health Sciences Council was convened for its one hundred twenty-first regular meeting on May 30, 2007 at 8:30 a.m. in the Rail Building, Rodbell Auditorium, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Dr. David Schwartz presided as Chair.

The meeting was open to the public on May 30, 2007 from 8:30 a.m. to 12:45 a.m. and in accordance with the provisions of Public Law 92-463 the meeting was closed to the public from 1:30 p.m. to 5:30 p.m. for consideration of grant applications. The meeting was reopened to the public on May 31, 2007 from 8:30 a.m. to 10:30 a.m. and in accordance with the provisions of Public Law 92-463 the meeting was closed to the public from 10:30 a.m. to 10:50 a.m. for consideration of grant applications. The meeting was reopened to the public from 11:00 a.m. to 12:00 p.m. Notice of the meeting was published in the *Federal Register*.

Members Present

Teresa Bowers, Ph.D.
Hillary Carpenter, Ph.D.
David Christiani, M.D.
Kathleen Dixon, Ph.D.
John Essigmann, Ph.D.
Elaine Faustman, Ph.D.
Joseph Graziano, Ph.D.

Stefani Hines, MS
George Leikauf, Ph.D.
Daniel Liebler, Ph.D.
David Losee, J.D.
Kenneth Ramos, Ph.D.
Peter Spencer, Ph.D.
Altaf Wani, Ph.D.

Members Present by Teleconference

Martin Philbert, Ph.D.

Members Absent

Bruce Freeman, Ph.D.
Lisa Greenhill, MPA
Kevin Stephens, M.D.

Ex Officio Members Present

COL James S. Neville

Liaison Members Present

Mo Mayrides, Ph.D., NIEHS Public Interest Liaison Group

NIEHS Staff

Kathy Ahlmark
Janice B. Allen, Ph.D.
Beth Anderson
Ralph Ball, Ph.D.
David Balshaw, Ph.D.
Linda Bass, Ph.D.
Perry Blackshear, Ph.D.
John Bucher, Ph.D.
Gwen Collman, Ph.D.
Allen Dearry, Ph.D.
Dorothy Duke
Sally Eckert-Tilotta, Ph.D.
Benigno Encarnacion
Christine Bruske Flowers
Elliot Gilmore
Kimberly Gray, Ph.D.
Thomas Hawkins
Heather Henry, Ph.D.
Marc Hollander
Michael Humble, Ph.D.
Laurie Johnson
Marian Johnson-Thompson, Ph.D.
Annette Kirshner, Ph.D.
Lacie Koppelman, Ph.D.
Dennis Lang, Ph.D.
Cindy Lawler, Ph.D.
Robin Mackar
Joyce Martin, J.D.
William Martin, M.D.

Carolyn Mason
J. Patrick Mastin, Ph.D.
Elizabeth Maull, Ph.D.
Kimberly McAllister, Ph.D.
Rose Anne McGee
Elizabeth McNair
Sirkanth Nadadur, Ph.D.
Teresa Nesbitt, Ph.D.
Liam O'Fallon
Michelle Owens
Jerry Phelps
Christopher Portier, Ph.D.
Leslie Reinlib, Ph.D.
Margarita Roque
John Schelp
Barbara Shane, Ph.D.
Daniel Shaughnessy, Ph.D.
Carol Shreffler, Ph.D.
William Suk, Ph.D.
Kristina Thayer, Ph.D.
Ann Thompson
Claudia Thompson, Ph.D.
Sally Tinkle, Ph.D.
Bennett Van Houten, Ph.D.
Brenda Weis, Ph.D.
Samuel Wilson, M.D.
Marva Wood
Leroy Worth, Ph.D.

Members of the Government Present

Ernie Takafuji, M.D., NIH/NIAD

Members of the Public Present

Maureen Avakian, Consultant
Christie Barker-Cummings, Social and Scientific Systems, Inc.
Patrick Crockett, Constella Group, LLC
Perry Kirkham, Ph.D., Purdue University
Susan Kinney, Integrated Laboratory Service, Inc.
Daniel Krewski, Ph.D., University of Ottawa
H. Troy Nagle, UNC-NCSU- Biomedical Engineering
Bobbie Peterson, RTI International
Anne Sassaman, Ph.D., Consultant
Pamela Schwingl, Social and Scientific Systems, Inc.
Michael Waters, Integrated Laboratory Scientific, Inc.

OPEN PORTION OF THE MEETING - May 30, 2007 - 8:30 a.m.

I. CALL TO ORDER AND OPENING REMARKS

Dr. David Schwartz called the one hundred twenty-first regular meeting of the National Advisory Environmental Health Sciences Council to order. He then asked the Council members to introduce themselves and welcomed the three new Council members, Drs. Hillary Carpenter, George Leikauf, and Kenneth Ramos. He then asked NIEHS staff and guests to continue with the introductions.

Dr. Dennis Lang reminded Council members to sign their Conflict of Interest forms and to complete their travel vouchers expeditiously. He noted that Michelle Owens was available to Council members to help with any administrative or logistic problems.

II. REVIEW OF CONFIDENTIALITY AND CONFLICT OF INTEREST PROCEDURES

Dr. Schwartz discussed with Council confidentiality and conflict of interest procedures and then read the requirements of the Government in the Sunshine Act and the Federal Advisory Committee Acts. All aspects of the meeting were open to the public except those concerned with review, discussion and evaluation of grant applications and related information.

III. CONSIDERATION OF MEETING MINUTES

The minutes of the February 15, 2007 meeting were approved as written.

IV. FUTURE COUNCIL MEETING DATES

The following dates were confirmed:

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|-----------------------|-------------------------|---------------------|
| September 17-18, 2007 | NIEHS | Monday - Tuesday |
| February 19-20, 2008 | NIEHS | Tuesday - Wednesday |
| May 13-14, 2008 | NIEHS (ONES Interviews) | Tuesday - Wednesday |
| May 29-30, 2008 | NIEHS | Thursday - Friday |
| September 9-10, 2008 | NIEHS | Tuesday - Wednesday |

V. REPORT OF THE DIRECTOR, NIEHS • Dr. Schwartz

Dr. Schwartz began his presentation with a discussion of the NIH budget, its importance globally and how it relates to NIEHS. He discussed the doubling of the NIH budget from 1998-2003 and subsequent leveling since 2003; however the number of applications has continued to increase. Therefore, it became necessary to identify core missions and to continue with the priorities already established. It also became necessary to try and leverage the dollars with other Institutes and agencies in order that the available dollars could allow the Institute to do more.

Dr. Schwartz highlighted several programs that were established relative to the Strategic Plan. Examples provided to Council were, the Discover Program (translational research), Director's Challenge (sabbatical to develop expertise in clinical research) and, the Ones Program (career development for young investigators).

Dr. Schwartz commented that the Institute would like to maintain the success rate at 20 percent for R01 s; the Institute will need to look carefully at the extramural portfolio and funding practices. He also pointed out the training programs the Institute is supporting, such as, the Steer Program (research training for high school and undergraduate students), the T32 Program (interdisciplinary research for pre-, postdoctoral, and physician scientist), T32 Partnerships with other Institutes (genomic research training for pre-and postdoctoral fellows), K12 Program (train physician scientists), K99/ROO (transition award, mentored to independent research) and the Ones Program (career development for young investigators). He also mentioned the Minority Career Development Program within the Intramural and Extramural Programs.

Dr. Schwartz outlined the partnerships that have been developed with NIH Institutes and other federal agencies. He stressed that these partnerships have been and will continue to be very important in terms of the impact environmental sciences will make on biomedical research.

Dr. Schwartz informed Council of two new developments. The first is the inquiry from the Congressional Oversight and Government Reform Committee and the second is the Roadmap Initiative in Epigenetics.

The Congressional Oversight and Government Reform Committee asked for information regarding the following:

- 1) The Environmental Health Perspectives Journal (EHP);
- 2) Budgetary information concerning the management of the Director's office; and
- 3) Personal information concerning interactions with outside organizations.

The Institute provided the information requested and a congressional response is expected in the near future. Dr. Schwartz commented on the need for more effective communication with the NIEHS and extramural communities.

A lengthy discussion ensued over the details of the congressional requests, Council's obligations, and Dr. Schwartz's response. Dr. Schwartz assured Council that he is providing all requested information and that he will keep Council informed regarding development on these issues.

The Epigenetics and the Microbiome Initiatives were selected for funding in the next iteration of the Roadmap and NIEHS and NIDA will lead the program. Dr. Schwartz noted that later in the Council meeting, Dr. Brenda Weis would present a detailed report of the initiative.

Council requested an update on EHP, and before the discussion began Dr. Schwartz recused himself due to conflicts of interest. Dr. Samuel Wilson then led the discussion. Dr. Wilson informed Council of the recusal process and that Dr. Raynard Kington, NIH Deputy Director, is the delegated authority to handle any issues concerning the EHP. Therefore, Dr. Kington has been working with Dr. William Martin concerning any issues that may arise. When Dr. Martin is not available Dr. Wilson interacts with Dr. Kington.

Dr. Wilson asked that the discussion be divided into two parts: the first part to conduct an item of business that was planned for discussion, and the second part to conduct a general discussion concerning EHP.

The business item pertained to plans to enhance EHP and to make it more effective as we move forward. Dr. Kington suggested that we conduct a "roundtable" or general brainstorming session in Washington, DC to more effectively get feedback, and gather information on

concerns and the future outlook for EHP. The individuals to be included would be from the community, press, and various individuals with interest in EHP. NIEHS would like to comply with this request by holding a roundtable meeting on June 27, 2007 in Bethesda, MD or surrounding area. We would like to conduct this meeting as a function of Council. We would like two Council members to participate and report the findings back to Council at the next meeting (September 2007).

Dr. Wilson then opened the second part of the discussion concerning EHP by stating that the current plan for EHP is for it to continue as a scientific journal funded at essentially the current level. The journal also will continue its community education and outreach features (news section).

Council then asked about the status of the editor of EHP. Dr. Wilson informed Council that the EHP editor would be a government employee, as in the past, and recruitment for this position will begin in the near future. Concerns were expressed regarding the expected qualifications of the editor. Dr. Wilson assured the Council that Dr. Martin, who has primary responsibility in the leadership of EHP, plans to recruit a candidate with outstanding scientific credibility, judgment, and independence.

Council requested that they be kept better informed in general, and specifically to know what the issues are related to EHP. Dr. Wilson described the issues under discussion concerning EHP; the first is whether there is justification for publishing the journal in light of the current budget climate. The second issue relates to whether the outreach and education portions of EHP could be covered by other mechanisms, e.g., newsletters and the Web. Third, there has been discussion on maintaining a level of investment in the journal that would be consistent with future opportunities and practices in scientific publishing. Council then discussed the need for balance in the content of EHP if a goal is still to reach the lay audience. Council continued to emphasize the need to be better informed on issues.

VI. BIODEFENSE RESEARCH at NIH and NIEHS - Drs. Takafuji and Maull

Dr. Ernest Takafuji (Director, Office of Biodefense at the National Institute of Allergy and Infectious Disease, NIH) presented an overview of the NIH biodefense program. He began his presentation by giving a brief description of weapons of mass destruction and what is included in this category (chemical agents, biological agents, radiological threats and the entire field of explosives). He noted that the Countermeasures Against Chemical Threats (Counter ACT) budget is approximately 50 million dollars and is a supplemental appropriation to the NIH 00 budget from Congress. This appropriation is expected to remain level over the next several years. This is a trans-NIH initiative in which the National Institute of Allergy and Infectious Diseases (NIAID) has taken the lead. The program is implemented through research grants, contracts, research agreements, and interagency agreements. The program is looking at therapeutic and diagnostic development as it relates to biochemical threats.

Dr. Takafuji then introduced Dr. Maull who presented the NIEHS Counter ACT portfolio. She pointed out that in 2006 four RFAs using the U01, U54, and U44 mechanisms were announced. The U01s are research projects, the U54 are Research Centers of Excellence and the U44s are Small Business Innovative Research contracts. The goals of these projects are to develop treatment therapies that will prevent or minimize disease processes to reduce morbidity and mortality as a result of chemical threat exposures, recognizing that an array of treatments specific to each stage of the pathology will be needed. The focus of the research is on

pulmonary effects in the areas of oxidative damage, inflammation versus repair, sensitivity versus resistance, and the impact of nerve agents. Dr. Maull pointed out the institutions involved in the research and the excellent interaction and collaborative efforts among the funded Centers. She noted that a Counter ACT meeting was held in April and was very informative for the participants. She then asked Council if they had any comments and questions concerning the presentation.

Council Response and Discussion

Questions focused on the type of technologies being developed. It was explained that NIH is focusing on biological systems; therefore the researchers are looking at diagnostic tools and not environmental sensors. NIH is looking at medical countermeasures, and the emphasis would be on interventions, protecting against the second wave, and long-term effects. Comments were made that this is a "sea change" for academic institutions that are doing research in this area because they will be expected to deliver a product at the end of their research.

VII. CHILDREN'S HEALTH RESEARCH EVALUATION - Drs. Thayer, Krewski, Collman

Dr. Thayer began her presentation by presenting an overview of the approach that was used to evaluate the Centers for Children's Environmental Health and Disease Prevention Research Program (Children's Center). She pointed out that the Children's Centers have been a prominent component of the NIEHS portfolio for the past decade and NIEHS and EPA, who co-fund the program, thought an evaluation of the program would be appropriate, at this time, to ascertain if maximum use and impact was being made with the research investment. The review panel was composed of scientists working in population-based research, the basic sciences, and a member from the public health advocacy community. The panel was charged with providing advice to Council on whether the Center's Program should continue in its present format or be changed, such as, altering the balance, other funding mechanisms, other research approaches, or do something different. The report was released for public comments in April 2007.

Dr. Daniel Krewski, chair of the review panel was then introduced. Dr. Krewski acknowledged the review panel members and gave the strengths and weaknesses of the current Children's Center Program.

The strengths are that the Centers promote visibility of children's environmental health and trans-disciplinary research (intellectual synergism between investigators from different disciplines); facilitate access to vulnerable populations; provide an infrastructure to respond to emerging risk issues (e.g., the World Trade Center); foster successful community outreach and; promote intervention, prevention and training.

The weaknesses are the narrow focus on local concerns; the limited number of health outcomes considered; less-than-optimal utilization of cohorts and other clinical resources (bio-repositories, etc.) by the scientific community; weaknesses in the basic science component in several key emerging areas (e.g., epigenetics, genome-wide analyses); and limited geographic representation.

Dr. Krewski outlined the suggestions the panel made, as follows:

Research focus should include etiology of children's environmentally-induced diseases at the cellular and molecular level; how life stages modify the effects of a chemical exposure; genetic and other biomarkers of individual susceptibility; multiple effects of the same pollutant; risks associated with exposures to mixtures of chemicals; effects of stresses on chemical exposures; biomarkers of exposure; gene-environment interactions; and new technologies to measure exposures in the field to both chemical and biological agents and to pinpoint the location of exposed individuals.

Required and Optional Center Components. The required components would include an administrative core; research support cores; strong basic science program with results directly linked to child health; and three or more externally funded research projects initially and five or more after three years to be eligible for renewal. Optional components would be community-based participatory research; training; and intervention/prevention programs.

Funding support would include planning grants to support development of the initial application to become a Center; projects should be externally supported primarily by R01 grants; funds should be designated for trans-disciplinary research grant focusing on basic science to address new problems in children's environmental health; Center core funding should be in the form of a grant rather than a contract; and supplemental Core funding should be available for training, community-based participatory research, and intervention/prevention.

Inter-Center Collaboration. The Children's Centers should function more as a national network to collectively address overall program goals; the scientific program should be broad to address most major children's environmental health issues; the Centers must address emerging children's environmental health issues; the underpinnings of the overall research program should be basic science; overlap and duplication among Centers should be avoided; and there is a need to broaden the geographic representation.

Application, Review and Renewal process. There should be an annual competition for the Centers, providing an ongoing opportunity for investigators to initiate new projects and programs; Centers would be funded for up to five years (renewable upon favorable review); and review criteria should include knowledge generation, trans-disciplinary knowledge translation, public impact, and inter-Center collaboration.

Partnerships. Wherever possible, Children's Centers should strive to build partnerships with other agencies and organizations which could include other child health research programs, both in the United States and abroad; major child health research initiatives, such as the National Children's Study and the National Birth Defects Prevention Study; hospitals and clinical facilities; government agencies, such as Centers for Disease Control; non-governmental organizations; public health associations; parent and child health advocacy groups; private foundations; community organizations; and international organizations, such as the World Health Organization.

Dr. Krewski ended his presentation by recognizing Drs. Kristina Thayer, Christopher Portier, Gwen Collman, David Schwartz, and Mr. Nigel Field for their invaluable input.

Dr. Schwartz introduced Dr. Gwen Collman who thanked the panel for their hard work and preparing a comprehensive report. She informed Council that NIEHS was looking at the pros and cons of the report to determine the best configuration for the future of the Children's Center Program. She noted that EPA is also reviewing the Children's Centers they support. They are looking at the output of the program as it relates to their program activities and the

Children's Centers have helped them with issues related to regulation and standard setting for the chemicals and toxic exposures related to this cohort.

Dr. Collman then introduced Drs. Graziano and Philbert, Council members, who provided comments concerning the report. They agreed with the report for the most part, except they are of the opinion that a better balance between the basic science and population-based studies is needed. A move toward a collection of R01 s is very problematic, however, and is not likely to achieve that goal. They pointed out that the strength of the Children's Centers has been in the population-based work, and the more outstanding Centers have also done related basic research. It is a disappointment that the community outreach and translation has been deleted and the community-based participatory research is optional; however, it is understood that some Centers do these components well and others do not.

Comments from the extramural community indicated they felt that movement away from community-based research and more toward basic research would jeopardize the cohorts that exist. Movement toward a consortium and basic science would jeopardize the ability of the Centers to leverage funding from outside sources. The timing and integration of reviews of R01 s at different study sections makes this approach completely infeasible. They noted that it is no longer an acceptable philosophy in science to collect specimens for biological repositories without engaging and involving the communities that provide them. In summary, there was disappointment with the composition of the committee, and it was felt that the outcome of the evaluation reflects the composition.

Council Response and Discussion

Council noted, while change is sometimes painful, there are some good things to take away from this report. A focus on basic science would advance the mission of many of the Centers, but need for balance should be recognized. The maintenance of the cohorts is a primary concern and should be considered carefully. If the Institute is to move toward the R01 mechanism and coalesce them into a Center, one has to think carefully how one bridges the already valuable and existing cohort that has been put together.

CLOSED PORTION OF THE MEETING

VIII. 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 Federal Advisory Committee Act, 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.

IX. Nanotechnology Research at NIEHS: An Update - Dr. Tinkle

Dr. Tinkle outlined the path taken to develop the Nanotechnology Research Program at NIEHS. In FY05 a Concept Clearance for an NIEHS Nanoscale Science Initiative was developed by a working group from the Division of Extramural Research and Training (DERT) and brought to Council for approval. After approval, Interagency Requests for Applications were developed.

In FY06, Human Health Effects of Manufactured Nanomaterials was a joint solicitation with Environmental Protection Agency (EPA), National Science Foundation (NSF), National Institute for Occupational Safety and Health (NIOSH), and National Institute of Environmental Health Science/National Institutes of Health (NIEHS/NIH). From this solicitation three applications were funded at 400,000 dollars per year for three years to look at cardiac toxicology, oxidative stress, and membrane dynamics.

In FY07 Manufactured Nanomaterials: Physico-chemical Principles of Biocompatibility and Toxicity was a joint solicitation, led by NIEHS, with EPA, NIOSH, National Cancer Institute, National Eye Institute, National Human Genome Research Institute, National Institute of Dental Craniofacial Research, National Institute General Medical Science as partners. NIEHS has allocated two million dollars per year for four years.

Dr. Tinkle mentioned the NTP activities in the area of Nanotechnology. Drs. Nigel Walker and John Bucher head the NTP Nanotechnology Safety Initiative. The research is evaluating dermal penetration *in vivo* and *in vitro* as well as phototoxicity and photocarcinogenicity using quantum dots as a surrogate for the titanium dioxide found in sunscreens; oral and pulmonary toxicity of carbon fullerenes; and pharmacokinetics and biocompatibility of dendrimers.

Dr. Tinkle then spoke about the next steps to be taken in this research area. NIEHS will continue to build on their investments and core competencies, and will continue to partner for integrated research success (trans-NIH activities and interagency collaborations). In doing so, the research should be consistent with United States goals for safe commercialization and innovation.

Dr. Tinkle noted that in May 2006, Dr. Zerhouni developed the trans-NIH technology task force. Its goal is to understand and facilitate the NIH research that is appropriate to the Federal agenda for commercialization and development of nanomaterials. The central goal is to decipher the fundamental principles of interaction between engineered nanomaterials (ENM) and biological systems that are relevant to human exposure and physiological response. The supporting goals are to develop tools and standards of practice for measuring and characterizing ENM in biological systems relevant to human health and to create an informatics resource for data sharing and analysis. She then pointed out, with this in mind, NIEHS has developed a NanoHealth Initiative to examine the fundamental physical-chemical interactions of nanomaterials with biological systems, at the cellular, molecular, and organ system levels, and their association with pathophysiological processes. There are five components to this initiative: materials science, basic biology, and pathobiology research; an informatics resource; and a training program.

Dr. Tinkle concluded her presentation on how the program will go forward in FY08. NIEHS will continue to work with collaborators and stakeholders. There will be a research symposium looking at translating data to information, and the NTP will propose initiatives looking at nanogold, nanosilver and multi-walled carbon nanotubes.

Council Response and Discussion

Council asked Dr. Tinkle if she would expand on the plans for public/private partnerships toward furthering this initiative. She informed Council that the Institute has been exploring several areas, such as identifying ways to foster partnerships where industry can contribute scientific ideas and money toward common research goals, and interacting with industry at major trade shows. Council thanked Dr. Tinkle for an informative presentation.

X. Adjournment

Meeting adjourned at 5:30 p.m.

OPEN PORTION OF THE MEETING - May 31, 2007 - 8:30 a.m.

XI. Concept Clearance - Global Environmental Health - Dr. Suk

Dr. Suk presented to Council the concept clearance for Global Environmental Health. He began by informing Council that NIEHS would like to develop a series of initiatives that address specific questions and problems relating to global environmental health. He pointed out that vulnerable populations have a right to be protected against environmental risks to their health, insufficient knowledge exists concerning environmental risks, and there is a shortage of researchers and clinicians trained in environmental health. Therefore, research, patient care, disease tracking, prevention, and training goals are needed. These goals must be linked to high-impact outreach strategy and guided by measurable results. The goals of the Concept fits into Goal IV of the NIEHS Strategic Plan: *Improve and expand community-linked research, develop a program in global environmental health, and build capacity to pursue research in global environmental health.* He mentioned that people in developing countries have diseases which are less prevalent in developed countries. However, more complex diseases such as heart disease and cancer are on the rise in developing countries. To address these problems we need, 1) better coordinated local and global data collection on environmental exposures in vulnerable populations related to health impacts and disease etiologies; 2) a global and strategic epidemiological effort to fill gaps in understanding the relationship between environmental exposures and poor health in vulnerable populations; and 3) better preventive measures to understand the mechanism and interactions between infectious diseases, environmental exposures, genetics, and predisposition. Dr. Suk pointed out that we need to increase coordination and collaboration amongst investigators worldwide to address the following questions: 1) which genes are important in human health? 2) What variants in these genes are relevant to risk of human disease? 3) How do these genes interact with other genes and the environmental to affect human health?

Dr. Suk concluded his presentation by emphasizing the need for global collaborations, coordination, and public/private partnerships to leverage funds for this initiative.

Dr. Suk then introduced Drs. Spencer and Essigmann, Council members, who reviewed the concept clearance. They thought that the Concept is an important initiative, and this is an opportunity for early discovery of developing diseases, treatment of chronic diseases, and training of environmental health scientists.

Council Response and Discussion

Council concluded that this concept is an excellent opportunity for research discovery of relevance not only to global health, but also to diseases that plague individuals within the United States. A motion for approval was made and seconded for the Concept and Council unanimously approved the Concept proposal.

XII. Concept Clearance - Undergraduate Diversity Training - Dr. Humble

Dr. Humble presented to Council the concept clearance for the NIEHS Undergraduate Diversity Training Program in the Environmental Health Sciences. He began his presentation with an overview of the program. The program falls under goal number six of the NIEHS Strategic Plan which is to recruit and train the next generation of environmental health scientists.

He noted the program will be targeted for undergraduates who fall under the NIH definition of diversity which would be individuals who are in the categories of underrepresented ethnic and racial groups, disadvantaged background, and disabilities. The T34 mechanism will be used and is new to NIEHS, but the program concept has been used for many years by the National Institute of General Medical Science (NIGMS) and the National Institute of Mental Health (NIMH). This will be a pre-baccalaureate undergraduate research training program in environmental health sciences for honors, junior, and senior students at minority and minority serving institutions. The goal is to increase the number and diversity of competitively trained undergraduates who can enter the PhD and MD/PhD programs in environmental health science.

Dr. Humble highlighted the components of the program. The program will provide didactic training as well as mentored research experiences. The trainees will be appointed at 12-month increments, ideally for two years and are expected to spend at least one summer in a research internship in the environmental health sciences at the applicant institution or at an approved external site. The program should have an evaluation and tracking component to follow students for a ten-year period to determine the success or failure of the program. Allowable cost would be a stipend for a 12-month appointment, tuition and fees, travel for the trainee to scientific meetings, workshops, and to a mentored research site. Allowable costs to the institution would be trainee-related expenses, curriculum improvement in the environmental health sciences, recruitment funds to strengthen the pool of potential trainees, and the cost to evaluate the program. It is hoped that applications can be received and reviewed by early spring and the results brought to May Council 2008 with an anticipated award date in the summer of 2008.

Dr. Humble then introduced Drs. Essigmann and Faustman, Council members, who reviewed the concept clearance. They thought that the concept fits well with the NIEHS Strategic Plan and targets students at a time when they are making decisions in the direction they want to proceed. However, there needs to be three clarifications in the RFA. First, the number of training positions requested by an institution should be in balance with the overall strength of the institution's undergraduate program. There needs to be clarity on how large or small a cohort of students is needed to provide this critical mass. Second, how will a sufficient base of environmental health related research be defined? With regard to this, clarification is needed about partnerships with other institutions, especially if the partner is with other minority institutions. Does the research base have to be at the minority institution or the host institution? Lastly, how will underrepresented and underserved be defined? Clear definitions need to be provided.

Council Response and Discussion

Council concluded that this concept is an excellent method to increase the pool of future researchers in the field of environmental sciences. A motion for approval was made and seconded for the Concept and Council unanimously approved the Concept proposal.

XI. Artificial Olfaction - Pattern Recognition by Biosensor Machines - Dr. Nagle

Dr. Schwartz introduced the seminar speaker Dr. H. Troy Nagle, who is chairman of the joint Department of Biomedical Engineering at the University of North Carolina at Chapel Hill and North Carolina State University at Raleigh. Dr. Nagle presented an overview of previous work he and his group has conducted on the development of a machine for artificial olfaction called the electronic nose (E-Nose). The concept is that the odorant is transported by the sampling unit onto the sensor array. The sensor responses are measured and sent to the signal processing unit for odor identification and/or characterization. Each sensor in the array has a unique broad response to profile to the spectrum of odorants under test. The pattern of response across the entire sensors in the array is used to identify and/or characterize the odor.

He then compared the human nose to the E-Nose. In the human system the turbinates take the incoming air, direct it across the olfactory mucosa, and there the trans-membrane receptors interact and transition information into the olfactory bulb and into the brain. The mammalian olfactory system employs thousands of sensors that the E-Nose is not able to duplicate. Therefore, the performance of artificial units can't duplicate that of mammals. The gold standard for odor measurement is a human panel of experts. Detection and recognition thresholds are established for populations of human subjects and are specified in odor units.

The E-Nose should possess the following characteristics: sensitivity, selectivity, stability, reliability, and affordability. Dr. Nagle summarized various types of technologies that are commonly used in constructing sensor arrays, such as conductivity sensors (metal oxides, conducting polymers), piezoelectric sensors (quartz crystal microbalance, surface acoustic wave), MOSEFTS, optical sensors, fast GC columns and mass spectrometry. Digital signal processing using pattern recognition methods is then used to extract odor characteristics from the sensor array's output waveforms.

Dr. Nagle concluded his presentation by giving examples of system concepts: a portable hand-held unit and the distributed array of RFID sensor platforms.

Council Response and Discussion

Council thanked Dr. Nagle for an interesting, stimulating, and informative presentation. One suggestion was offered, that of adding specific biosensors to the E-nose sensors array.

CLOSED PORTION OF THE MEETING

XIII. Consideration of Grant Applications

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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).

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OPEN PORTION OF THE MEETING

XIV. Epigenetics Roadmap Initiative - Dr. Weis

Dr. Weis acknowledged the trans-NIH group that was charged to develop a research program that would transform biomedical research in the next ten years. The group looked at several possibilities and chose epigenetics which has the criteria they were looking for and is an emerging science. She defined epigenetics as having heritable traits that are not dependent on DNA sequence. The primary mechanism is DNA methylation or silencing of genes through cytosine methylation within CpG motifs. Others include noncoding RNAs (siRNAs) which interfere with transcription and post-transcriptional regulation of gene expression, and histone modification through methylation, acetylation, or phosphorylation which in this case are post-translational modifications. She noted there is compelling evidence that the epigenetic mechanism plays a role in human health and disease and gave several examples: dietary supplementation and its effect on methylation status in mouse embryos that is then maintained as adult phenotypes; epigenetic markers show disease activity, such as reduced methylation and acetylation of histones which can predict risk of recurrence in the early stages of prostate cancer; and they may help in the development of therapies that aid in the recovery of learning and memory in patients with neurodegenerative disease. Dr. Weis pointed out that there are opportunities to develop new technology as tools to measure epigenetic changes, particularly since the genome is not represented on any single microarray.

She noted that there is little disease-focused research in the NIH epigenetics portfolio, except in cancer. There are many research opportunities open to NIEHS and other institutes and a number of international programs are very active in epigenetics, but a lack of integration, organization, and leadership exist within and across the NIH and international programs. Limitations were noted, such as, no publicly accessible database, few available reference epigenomes, little investment in disease-focused research other than cancer, and limited tools to measure epigenetic changes across the genome, and for imaging epigenetic changes within single cells, tissues, and whole animals. The program proposes to establish an infrastructure composed of four components: 1) an NIH-led international consortium; 2) creation of reference epigenomes; 3) publicly accessible epigenetic database; and 4) new technology to meet the needs of genomic-wide analysis at a high level of resolution and to capture epigenetic events *in vivo*. Three million dollars has been allocated in FY07 to "jumpstart" the creation of the international consortium, initiate development of the public database, and to identify standardized protocols and reagents for epigenomic research, etc. Four RFAs have been proposed. Three are scheduled for release in FY08: the Epigenomic Mapping Centers, Data

Management Center, and technology development and one in FY09 that involves projects that are co-funded by Roadmap and the ICs (Epigenetics of Human Health and Disease).

Dr. Weis concluded her presentation outlining the proposed Epigenetics Program budget and funding period. The Epigenetics Working Group requested 248.5 million dollars for ten years. However, it is unknown at this point what the actual budget and period of funding will be, as a decision has not yet been made by the NIH Office of Portfolio Analysis and Strategic Initiatives (OPASI).

Council Response and Discussion

Council discussed various avenues to enhance the Epigenetics Program. The suggestions were noted by Dr. Weis. She informed Council that the Institute would explore their suggestions. Council thanked Dr. Weis for an informative presentation.

XV. Report of the Interim Director, **DERT** - Dr. Lang

Dr. Lang began his presentation with the Council Delegated Authorities which is normally presented at the February Council for approval. However, a new requirement in the NIH Reauthorization Act brings it to this Council for approval. The Act mandates that all research grants and cooperative agreements must undergo Advisory Council/Board review and approval prior to funding, including applications \$50,000 and under in direct cost. NIEHS previously had authority to make decisions without Council approval on awards \$50,000 and under in direct cost. Therefore, approval of the change in Council Delegated Authorities was requested from Council. A motion for approval was made and seconded and Council unanimously approved the change in the Council Delegated Authorities.

Dr. Lang then listed the topics he would be discussing: the Breast Cancer and the Environment Research Centers (BCERC) Working Group Report; the disaster preparedness training; the Superfund Basic Research Program (SBRP) Risk e-learning seminars; and the International Training in Research in Environmental and Occupational Health (ITREOH) Program Report.

The BCERCs consist of four centers (Fox Chase Cancer Center, Michigan State University, University of California, San Francisco, and the University of Cincinnati). Each Center has outside collaborators and community partners. NIEHS co-funds these Centers with NCI, and the Avon Foundation contributes to meeting support and publication costs. The BCERC Working Group Report noted the Centers were meeting their goals but expressed concern in several areas: 1) low rate of publication; 2) the small cohort of girls with a family history of breast cancer (University of Cincinnati) not provide clear data although the statisticians indicate otherwise; 3) blood collection practices across Centers need to be made consistent; 4) epidemiological studies found unexpected high levels of perfluorinated hydrocarbons and need to look closer at this group of compounds, and 5) the Community Outreach and Training Cores (COTC) need to seek additional funding to expand to target audiences, to develop an information dissemination plan in advance of new findings that are likely to emerge, and to produce manuscripts with laboratory and epidemiology investigators. Dr. Lang acknowledged the working group committee.

Dr. Lang presented an update on disaster preparedness training. As part of the National Response Plan, NIEHS Worker Education Training Program (WETP) is tasked with preparing curricula and providing safety and health training for responding to natural and man-made

disasters. WETP has recently become involved in two new areas, avian influenza and radiological dispersion (dirty bombs).

He informed Council that an online web-based seminar series called Risk e-learning has been developed by the SBRP in conjunction with EPA. The objective of the seminar series (which are presented live) is to translate basic and applied SBRP research to EPA risk assessors and remedial project managers, and to other SBRP stakeholders.

Dr. Lang concluded with the ITREOH Program Report. This is a collaborative program involving Fogarty International Center, NIEHS, and NIOSH, which began in the mid-1990s. The goal of the program is to develop infrastructure and training activities in foreign countries. He then outlined the results from the current solicitation. Thirty-two applications were received, seventeen were competing continuations and 15 were new applications. Sixteen applications (14 competing continuation and two new) were recommended for funding at a total cost of \$2,322,000. NIEHS contributed \$600,000 to this initiative.

XVI. Report of the Interim Director, Division of Intramural Research (DIR) - Dr. Blackshear

Dr. Blackshear informed Council that the National Toxicology Program (NTP) was prepared to present an example of translational research; however, in the interest of time the presentation by Dr. William Copeland will be postponed until the September Council meeting. He then acknowledged Dr. Joel Abramowitz for the report on DIR that was included in the Council package.

Dr. Blackshear concluded by updating Council on the Clinical Research Unit. It is anticipated that the clinical building will be completed by late July. Also, NIEHS is recruiting two individuals; one is a staff clinician who will be the onsite administrator and the other is a clinical scientist with expertise in the area of reproductive endocrinology

XVII. Report of the Interim Associate Director, National Toxicology Program (NTP) - Dr. Dearry

Dr. Dearry provided Council with an overview of NTP. The purpose of NTP is to coordinate toxicology testing programs across the Federal government, to develop new approaches to toxicology, including improved testing methods, and to insure that NTP provides all the information from their findings to help regulatory research, scientific and medical communities, and the public. NTP has a director, a committee that deals with policy oversight, called the Executive Committee which is composed of the Agency for Toxic Substances and Disease Registry/National Center for Environmental Health (ATSDR/NCEH), Consumer Product Safety Commission (CPSC), Environmental Protection Agency (EPA), Food and Drug Administration (FDA), National Cancer Institute (NCI), National Institute of Environmental Health Sciences (NIEHS), National Institute of Occupational Safety and Health (NIOSH), and Occupational Safety and Health Administration (OSHA), and a Board of Scientific Counselors which provides scientific oversight, peer review, and guidance to NTP.

Dr. Dearry outlined the NTP research and testing program, the NTP roadmap, and the analysis and assessment activities. He gave an overview of the NIH Molecular Libraries Initiative (MU), with which NTP is a partner on high-throughput screening (HTS), and the Host Susceptibility Initiative.

The MLI uses HTS to identify small molecules that can be optimized as chemical probes to study functions of genes, cells, and biochemical pathways. NTP has an established collaboration with the NIH Chemical Genomics Center (NCGC), and supplied chemicals and assays to MLI. The NTP is developing tools to link data generated from HTS assays to data produced by the NTP's toxicology testing program. Further development is focusing on critical pathways in immune function and cancer.

The Host Susceptibility Initiative proposes to study the genetic basis underlying biological response, utilize multiple strains of inbred mice or GMMs, exploit findings from NTP 15 isogenic mouse strain single nucleotide polymorphism (SNP) analysis (> 8 million SNPs), and to provide data to allow identification of quantitative trait loci (QTL) with selected biological responses. This initiative will include partnering with intramural and extramural scientists. Current efforts are focused on optimal design and staffing of the program.

Dr. Dearry concluded his presentation by giving an update on three of the assessment/analysis activities. The first is the Report on Carcinogens (RoC). NTP has been coordinating with OMB to develop a new review process for nominations to the 12th RoC. The review process will involve public peer review by ad hoc scientific expert panels, as well as peer review of the draft substance profiles by the Board of Scientific Counselors. The RoC review process has been announced in the *Federal Register* and expert panels are being recruited. The second is the Center for Evaluation of Risks to Human Reproduction (CERHR) which has examined 20 chemicals, such as phthalates, acrylamide, styrene, soy formula, genistein, and hydroxyurea. Bisphenol A is currently being evaluated. The review started with an initial expert panel that met in March. The same expert panel is scheduled to meet again in August to finish their deliberations and finalize the report. The third analysis activity is the NTP Interagency Center for Evaluation of Alternative Toxicological Methods (NICEATM), which assists in developing, reviewing, and validating improved test methods aimed at reducing, refining, or replacing the use of animals in toxicity testing. There are a number of ongoing activities related to improving endocrine disrupter screening, and *in vitro* ocular toxicity methods. A strategic plan is being developed which is intended to guide this activity through its research, validation, and translation for the next five to ten years.

Council Response and Discussion

Council thanked Dr. Dearry for his informative presentation.

XVIII. CLOSING REMARKS - Dr. Schwartz

In closing, Dr. Schwartz noted that Council would like to extend the second day of September Council to 2:00 p.m. or 3:00 p.m. NIEHS staff will look at the schedule to see if the request could be accommodated. Dr. Schwartz gave special thanks to Dr. Lang and Ms. Elizabeth McNair for their efforts in organizing a paperless, all electronic council. He also thanked everyone for their contributions to the Council discussions and deliberations.

XIX. ADJOURNMENT OF THE NAEHS COUNCIL

The meeting was adjourned at 12:00 p.m. on May 31, 2007

CERTIFICATION

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

Samuel H. Wilson, M.D.
Chairperson
National Advisory Environmental
Health Sciences Council

Denni Lang, Ph.D.
Acting Executive Sec' tary
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Attachment:
Council Roster

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May 25, 2007

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