

**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
September 13, 2005**

The National Advisory Environmental Health Sciences Council was convened for its one hundred sixteenth regular meeting at 8:30 a.m. on September 13, 2005 in the Rall 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 September 13, 2005, from 8:30 a.m. to 1:00 p.m. in accordance with the provisions of Public Law 92-463. The meeting was closed to the public on September 13, 2005, from 1:00 p.m. to 4:00 p.m. for consideration of grant applications. Notice of the meeting was published in the Federal Register.

Members Present:

Douglas Benevento, J.D
Teresa Bowers, Ph.D.
Kathleen Dixon, Ph.D.
Elaine Faustman, Ph.D.
Bruce Freeman, Ph.D.
Bernard Goldstein, M.D., Ph.D.
Lisa Greenhill, MPA
Daniel Liebler, Ph.D
David Losee, J.D.
Martin Phillbert, Ph.D.
Peter Spencer, Ph.D.
Frank Talamantes, Ph.D.
James Townsel, Ph.D.

Members Absent

Deborah Brooks
Charli Coon, J.D.
George Gray, Ph.D.
Peter Thorne, Ph.D.

Ex Officio Members Absent

COL James S. Neville

Liaison Members Present

George Corcoran, Ph.D. - Alternate (Society of Toxicology)

Liaison Members Absent:

Drue Barrett, Ph.D. (National Center for Environmental Health, ATSDR, CDC)

David Ringer, Ph.D. (American Cancer Society)

Michael Galvin, Ph.D. (National Institute for Occupational Safety and Health)

Hal Zenick, Ph.D. (National Health & Environmental Effects Research Laboratory, USEPA)

NIEHS Staff

Janice B. Allen, Ph.D.

Beth Anderson

Lisa Archer

David Balshaw, Ph.D.

Amber Barnes

Martha Barnes

Linda Bass, Ph.D.

Robert Berendt

Lutz Birnbaumer, Ph.D.

David Brown

Christine Bruske

Gwen Collman, Ph.D.

Allen Dearry, Ph.D.

Dorothy Duke

Donald Ellis

Sally Eckert-Tilotta, Ph.D.

Richard Freed

Mary Gant

Kimberly Gray, Ph.D.

Jerrold Heindel, Ph.D.

Joseph Hughes

Michael Humble, Ph.D.

Ethel Jackson, D.D.S

Laurie Johnson

Marian Johnson-Thompson, Ph.D.

Charle League

Dennis Lang, Ph.D.

Robin Mackar

Elizabeth Maull, Ph.D.

Carolyn Mason

J. Patrick Mastin, Ph.D.

Kimberly McAllister, Ph.D.

Rose Anne McGee

Pamela Moore

Kim Minneman

Teresa Nesbitt, DVM, Ph.D.
Sheila Newton, Ph.D.
Liam O'Fallon
Michelle Owens
Theodore Outwater
Jerry Phelps
Leslie Reinlib, Ph.D.
Margarita Roque
Anne P. Sassaman, Ph.D.
Shobha Srinivasan, Ph.D.
William Suk, Ph.D.
Anne Thompson
Claudia Thompson, Ph.D.
Patricia Thompson
Sally Tinkle, Ph.D.
Frederick Tyson, Ph.D.
Bennett Van Houten, Ph.D.
Brenda Weis, Ph.D.
Charles Wells, Ph.D.
Samuel Wilson, M.D.
Leroy Worth, Jr., Ph.D.

Other Federal Staff

Rosemary Springer, Food and Drug Administration

I. CALL TO ORDER AND OPENING REMARKS

Dr. David Schwartz called the one hundred sixteenth regular meeting of the National Advisory Environmental Health Sciences Council to order. Dr. Schwartz, in his opening remarks, informed Council that their comments would be very beneficial in charting the next six months of development at the Institute. He would be soliciting Council's feedback on changes the Institute was considering.

He informed Council that Dr. Douglas Benevento was participating in the meeting via teleconferencing and that the following members were absent from the meeting: Drs. Peter Thorne, James Neville, Ms. Deborah Brooks, and Ms. Charli Coon. He recognized Dr. George Corcoran who was a representative for the Society of Toxicology (SOT). He noted that five members were retiring. Certificates for Appreciation of Service were presented to Drs. Bernard Goldstein and James Townsel. Ms. Deborah Brooks, Ms. Charli Coon, and Dr. George Gray will receive their certificates by mail. Dr. Schwartz stated that the five retired members of the Council will be replaced over the next 6 months. He expressed his gratitude to the retiring members for their service to Council and he was looking forward to their continued involvement with the Institute. He then had the Council members, NIEHS staff and guests introduce themselves.

Dr. Anne Sassaman brought to the attention of Council that Ms. Michelle Owens was available to assist them on any administrative matters. She also reminded Council members to sign their Conflict of Interest forms and to complete their travel vouchers expeditiously. Dr. Sassaman also pointed out that in their packets was a CD about one of the SBIR grants. She said it was quite informative and urged Council to take a look at it.

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 May 26, 2005 meeting were approved as written.

FUTURE COUNCIL MEETING DATES

The following dates for February and June were confirmed

February 16-17, 2006; NIEHS, Thursday - Friday

June 1-2, 2006; NIEHS, Thursday - Friday

September 18-19, 2006; NIEHS, Monday - Tuesday

IV. REPORT OF THE DIRECTOR, NIEHS - Dr. David Schwartz

Dr. Schwartz began his presentation by stating that Council members should feel free at any time during the presentation to ask questions or have statements clarified. He informed Council that his presentation would not include the budget, although if Council wished to hear or ask question concerning the budget he was prepared to address any issues they might have. He thought it would be most helpful for the Council to be brought up to date with the progress NIEHS has made over the last several months and the programs that the Institute is currently working on.

Dr. Schwartz acknowledged Drs. Samuel Wilson, Lutz Birnbaumer, Anne Sassaman, Allen Dearry, Brenda Weis, and, Ms. Kim Minneman who have helped push forward the progress and development of the Institute over the past several months. He acknowledged that others also contributed to this overall effort.

Dr. Schwartz outlined his presentation in the following order: Strategic Planning, Prioritizing and Program Development, Trans-NIH Initiatives, Center for Scientific Review, NIH Reauthorization and Hurricane Katrina.

Dr. Schwartz noted that NIEHS has had a tremendous number of accomplishments in the area of basic science and in public health, but the area that is somewhat deficient is integrative or translational research and clinical research as it relates to specific diseases. Under Ken Olden's

direction there has been a tremendous movement towards focusing on these activities, but the Institute plans to refocus these efforts on more integrative approaches to basic research and clinical research. The Institute plans to incorporate the strengths that already exist in basic biology and public health as a continuum to an integrative program in the extramural research programs as well as the intramural research programs.

Dr. Schwartz spoke about the vision for NIEHS and noted that at the last Council meeting (May) the Institute envisioned moving towards the use of environmental sciences to understand human disease and improve human health. At the last Council (May) it was noted that this vision appeared to be a "Sea Change". Dr. Schwartz agreed with the perception that the Institute is shifting its emphasis from the traditional approach to a new approach. The traditional approach, at NIEHS, was to use environmental exposure to understand basic science and toxicology, to understand public health in terms of distribution of disease in populations, and subsequently to understand human diseases by inference or by progressive investigations that began in terms of basic toxicology and basic public health. This is somewhat circuitous if we want to affect human disease. Therefore, we wish to develop and support programs that more directly relate to human disease with specific exposures. We think that if we focus on this relationship between exposures and disease, which is obviously a bidirectional relationship, we will be able to then derive biology that is relevant to human disease. This new approach will lead to understanding how diseases are distributed in populations.

However, Dr. Schwartz emphasized that the Institute is not moving away from its commitment to public health or its commitment to basic science and toxicology but plans to focus on the relationship between exposures and human disease as a way of primarily being able to understand the pathogenesis and etiology of complex human diseases, which account for between 70% and 90% of diseases that Americans develop.

Dr. Schwartz then informed Council that the Institute is in a strategic planning process and Dr. Sheila Newton will outline the process in detail during her presentation. He mentioned that a solicitation was published in the Federal Register and a website was established to allow individuals to send in suggestions about various aspects of the Institute's portfolio and the direction the Institute is taking in hopes of providing questions for the Strategic planning meeting scheduled for October 17-18. NIEHS plans to use that meeting to develop a document, available for public comment, summarizing many of the priorities and the programs that those priorities will involve. Thus, this will be a blue print that the Institute will follow over the next three to five years. It is expected that a final document will be available early 2006.

Dr. Schwartz spoke to how the Institute is prioritizing and developing new programs. He pointed out that the Toxicogenomics consortium and Mouse Genomic Centers will not be renewed. Those programs will close out in mid 2007. Due to the wide availability of genomic technology it is no longer necessary to develop technology in this area.

The Children's Centers have gone through two cycles of funding and this program will sunset at ten years. Dr. Schwartz emphasized that while the Institute remains committed to children's environmental health, the program needs to be re-evaluated, re-assessed, and re-equilibrated.

New plans are being formulated for Centers that will encompass Children's environmental health.

Environmental Health Science Research Centers (EHSRC) have been revised substantially. Those Centers will focus more on human disease and human health related issues. Dr. Sassaman will go into greater detail during her presentation.

Dr. Schwartz described some of the new areas/initiatives in the process of being developed: enhancing flexibility for investigators, programs that focus on human disease and pathogenic endpoints, and integrating basic and clinical research.

Dr. Schwartz also informed Council that the Division of Intramural Research's (DIR) structure and function was in the process of evaluation to create a much more integrated program and to focus on various pathogenic processes that are relevant to environmental diseases.

Dr. Schwartz spoke about the Exposure Biology Initiative. This initiative is being proposed in order to develop precise measures of environmental exposure that will allow investigators to look more critically at environment biology interactions that allow one to understand how the environment is contributing to the development of disease. In terms of infrastructure development, these tools are extremely important and are applicable to many different studies and disease processes that are relevant not only to NIEHS investigators but to investigators outside of NIEHS. Dr. Schwartz acknowledged Dr. Brenda Weis's help in creating this initiative. A conference is proposed that will focus on the Exposure Biology Initiative. Fifty to sixty people will be invited to assist in outlining the issues and identifying some of the directions the initiative should take. RFAs are proposed for sometime either in late 2006 or early 2007.

Dr. Schwartz addressed the need to increase the number of physician-scientist. He pointed out that if we are really intent on affecting human disease and human health we have to increase the number of physician-scientists. In the next five years we would like that number to increase to 30% of the principal investigators in our portfolio. The number currently is around 21% to 22% for NIEHS. To do this, the Institute has developed an R01 program that focuses on using environmental science as a way of understanding human disease and also focuses on helping young investigators start up their laboratories. The plan is to expand the K12 career development program. The K12 program is a program that helps individuals move from training, mentored research to independent research or postdoctoral to young faculty positions. We would like also to re-engineer the T32 program so that it can incorporate more physician-scientists into those programs.

Dr. Schwartz highlighted some of the trans-NIH initiatives in which the Institute is involved, such as the Roadmap initiative, collaborations with colleagues in the National Human Genome Research Institute and with the National Institute of Child Health and Human Development.

The Roadmap initiative is expected to grow over the next several years. Dr. Schwartz co-chairs the interdisciplinary roadmap program along with Dr. Lawrence Tabak and Dr. Dennis Lang is the Institute representative for Roadmap activities. Some of the Roadmap activities that we are involved in are nanotechnology and re-engineering the workforce.

The American Gene by Environment Study (AGES) is being proposed primarily by the National Human Genome Research Institute with NIEHS to look at disease endpoints in 500,000 individuals over a 15-year period, to understand how genes and environmental exposures contribute to the risk of developing disease.

The third trans-NIH Initiative is The National Children's Study (NCS). This proposal from the National Institute of Child Health and Human Development plans to study 100,000 pregnant women through their pregnancy and for the first 10-15 years of their child's development, again to identify how environment and gene variation contribute to the development of disease. In looking at the AGES and NCS studies the importance of more precisely measuring exposures was evident both in terms of what someone is exposed to (environmental sensors) and their biological response to exposure (biosensors). In either case, technology development may be necessary. Dr. Zerhouni was very enthusiastic about these possibilities and thought the AGES and NCS studies should be merged together as one study. NIEHS proposed a Technology Development Core to help develop the Exposure Biology Initiative that would be applicable to both of these studies. A combined study AGES - NCS with a number of shared resources, including the Technology Development Core that NIEHS would take the lead in developing has been presented to the office of the Secretary, DHHS. Hopefully this would bring in new money to NIEHS directly from the Secretary. The cost of this study is \$5.6 billion. However, NIEHS is committed to the Exposure Biology Initiative with modest funds.

Dr. Schwartz informed Council that NIEHS has been working with the Center for Scientific Review concerning the way study sections have been reorganized, and a proposal has been developed and sent to Dr. Anthony Scarpa for his consideration. We are proposing an Integrated Review Group (IRG) in environmental health sciences. The purpose of this IRG would be to review applications focusing on the role of environmental exposures and in understanding human biology and human disease. Dr. Schwartz reminded everyone that this is only a proposal and has not been finalized. This IRG would review not only applications that are assigned to NIEHS grantees, but also from those assigned to other Institutes; this is not to be an NIEHS-directed IRG.

Council felt that this was an important issue and drafted a statement that will be sent to Dr. Scarpa in support of this IRG.

Dr. Schwartz gave Council an update on the NIH Reauthorization bill. He informed Council that the bill has not yet made it to the floor of Congress and many parts of this bill will not be going forward. The part that is going forward is the creation of an Office of Portfolio Analysis and Strategic Initiatives (OPASI) which represents an extension of the NIH Roadmap. A case has been made by Dr. Zerhouni and others to Congress that this Office would be more effective than Institute-directed research in terms of focusing on emerging scientific opportunities that are trans-NIH opportunities, which address issues in public health and involve multiple institutes. Basically the plan currently is to start the Office at about 1% of the NIH budget and eventually reaching 5% of the NIH budget by 2010 or 2011. This is a substantial amount of money. Therefore, the NIEHS needs to develop strategies to gain a portion of these funds, as a way of bringing new money to our investigators. It should be noted that the ICs will still maintain their individual appropriations.

Dr. Schwartz concluded his presentation with an update on the response to Hurricane Katrina by NIH and NIEHS. NIH responded by admitting patients to the Clinical Center in Bethesda, Maryland, developing consultative services at the NIH involving partners in the Association of American Medical Colleges (AAMC) with medical schools throughout the country, and sending a relief effort to Meridian Mississippi. Of approximately 50 individuals, about 20-25 were from the Bethesda, Maryland campus, 20-25 were from NIEHS and Duke University. The hospital in Meridian Mississippi was about 200 miles away from the eye of the hurricane and people affected really did not want to leave the area near their homes. Therefore, the team went down to the coast, Gulfport and Waveland. After a week it was decided that the team would return home because individuals were getting the kind of care they needed through DMAT (Disaster Medical Assistance Team) units that are deployed by FEMA (Federal Emergency Management Agency), through the local health care systems, and from hospitals throughout the region.

At NIEHS we have three different initiatives related to the Hurricane Katrina disaster. A website has been developed in collaboration with investigators at Duke and the University of California, San Diego. We are in the process of supporting efforts by the Center of Disease Control and Prevention (CDC) that is deploying public health units throughout the region; Dr. Mary Wolfe from the National Toxicology Program is currently working with Dr. Thomas Sinks at the CDC to help coordinate activities between NIEHS and the CDC. We are in the process of developing a research initiative that could directly address the health concerns, health needs and exposures for individuals in that region.

The Hurricane Katrina website was displayed for Council to see the first iteration of maps that indicate the potential toxicant sources throughout the region. More comprehensive 3-dimensional maps are being developed that will allow us to drill down to identify the exposures at each site. While these maps will not provide the precision that is needed to identify whether exposures are affecting health in the population, this is a starting point, to focus our attention on particular areas, groups of individuals or agents that might be relevant to the health effects of exposures that occur as a result of this disaster in the Gulf region.

Council Response and Discussion

Throughout the Director's presentation, Council asked questions for information and/or clarification.

There was concern that if NIEHS focused on specific diseases we would lose the interactions that toxicants and environmental influences have on multiple organs which in turn cause multiple diseases. It was clarified that we would not be addressing specific diseases but disease processes and common pathways.

A Council discussion centered on the need to train more physicians to be good research scientists by giving them the necessary research skills versus the need to train PhDs in the basic medical sciences. It was concluded that it would be good if both had training in both directions and worked side-by-side in the training process, as well as being mentored by scientists from different disciplines.

Concern was expressed about the ethical problems that are associated with large studies where enormous amounts of very personal data are generated and, through the use of modern technology, can be disseminated to both authorized and unauthorized individuals. It was acknowledge that this was a concern and would be addressed at the strategic planning meeting.

Council expressed their appreciation for the dialogue between CSR and NIEHS on the proposed IRG in environmental health sciences. They thought this IRG is long overdue and is important to the grantees.

Clarification was given on the allocation to OPASI. Initially this will be 1% of the NIH budget. It was noted that this initial 1%, eventually 5%, is separate from the 1% reallocation authority that the NIH Director has, so these monies are above and beyond the 1% that are at the discretion of the NIH Director.

V. Strategic Plan and Benchmarking - Drs. Shelia Newton and Benjamin Van Houten (Attachment 2)

Dr. Newton presented the strategic planning initiative that has been a priority on Dr. Schwartz's agenda. The last time a strategic planning initiative was done was in 2000 under the request of Dr. Harold Varmus, the NIH Director. The Institute sees this as an opportunity to engage extramural and intramural investigators and other scientific and public health leaders in focused discussions to identify future basic and clinical science priorities related to environmental health. We want to identify areas where the assets, expertise, and outreach of the Institute can be directed to achieve the greatest impact. The intent is to develop a clear strategic plan for NIEHS to guide and support future program planning and research investment.

Dr. Newton gave an update on the planning process. Over 500 scientists, clinicians and stakeholders responded to a six-question web survey on future needs and program options. These responses are being adapted into an agenda for the NIEHS Strategic Planning Forum, to be held in Chapel Hill on October 17-18. Approximately 90-100 scientist and clinicians representing multiple disciplines and points of view will attend. The final document will be completed in February 2006.

Dr. Van Houten began his presentation of the NIEHS Portfolio Benchmark Analysis by outlining the topics of discussion which are: goals of the project, the process, data collection, and questions for the council subcommittee. He informed Council that the analysis was undertaken to understand our portfolios in respect to the other ICs. Several institutes were selected which are of similar size and have broad missions. They are the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Child Health and Human Development (NICHD), the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), and the National Institute of Alcohol abuse and Alcoholism (NIAAA).

The process began in June 2005. The working group consisted of DERT extramural staff which met weekly to develop data and questions. The data and questions were then submitted to a subcommittee of NAEHS to evaluate and give feedback at the February 2006 Council.

Data were collected to see how we were spending money compared to other institutes, broken out in terms of mechanisms. We also wanted to look at the following: targeted research versus non-targeted research, how we balance the spending in these two areas; how our success rate compared to the other institutes; our science distribution and impact, and how the portfolios have changed over time.

The following questions were submitted to the Council subcommittee to answer over the next two days:

1. How have we spent monies over the last ten years; has this helped NIEHS achieve its mission and has the monies spent been appropriate to achieve our mission?
2. Has the Centers program investment relative to unsolicited RPGs been appropriate and justified; are we spending the appropriate amount for Centers?
3. Is our current level of support for training adequate? Should we be spending more or less; should existing programs be modified; and is there a need for new programs?
4. Is there an adequate balance between targeted and non-targeted applications? Has the success rate for non-targeted research been adequate? In times of flat budgets, how do we maintain the ability to fund targeted research?
5. Is NIEHS investing too heavily in certain areas of science? Should we be investing more in other areas of science? Is any area of science missing that we should be investing in?
6. Are we translating our scientific research to the medical and lay public? What are the best measures of success?
7. What mechanism would you suggest to attract and fund new investigators?
8. What type of data would you like to see tracked and reported on a regular basis concerning NIEHS portfolios?

Dr. Van Houten concluded his presentation by informing Council that, the subcommittee will report on the above questions at the next meeting. He encouraged Council to feel free to continue asking questions as more data is generated from this benchmarking process.

Council-Initiated Discussion

Council requested copies, if they were available, of the strategic plans from other Institutes. They also requested the analysis of the six questions from the web-site. Council was interested in what outcomes were expected from the strategic planning process and what process will be used for monitoring impact on initiatives that will come out of the strategic plan.

Council was interested in how the benchmarking activity related to the strategic planning activity. Dr. Schwartz informed Council that the benchmarking process will consider distribution and allocation of resources within the portfolios, and the strategic planning process will address investigative opportunities in the field of environmental health sciences. These activities are running parallel and, at times, will overlap

VI. Report of the Director, DERT - Dr. Anne Sassaman

Dr. Sassaman began her report by thanking the Benchmark team for all their efforts and for a job well done. She also informed Council that Dr. Shobha Srinivasan would be departing NIEHS at the end of the month to be Coordinator of the Health Disparities Program for the National Cancer Institute.

Dr. Sassaman updated Council on the FY05 Extramural Loan Repayment Program, the RFA for the Outstanding New Environmental Scientist Award (ONES) program, and the Epigenetics Program. She informed Council that the Loan Repayment Program funded 8 pediatric and 8 clinical investigators in the amount of \$464,360. The ONES program is viewed as a pilot project and has generated a great deal of interest from the extramural community. It is a mechanism designed to bring outstanding investigators into the field. After the review the top candidates will be invited to NIEHS to present their work before final selections are made. Council was thanked for working on the Concept Proposal for the Epigenetic Program during their recess and was informed that the RFA is being processed. The RFA for Integrative Environmental Health Research Concept Proposal that was presented at the last Council (May) by Dr. Mastin is also being processed.

Dr. Sassaman highlighted the response NIEHS made to the extramural community affected by Hurricane Katrina. The extramural staff has been in communication with investigators and institutions on what we can do and what we are doing in terms of institutional support. We have set up a process to help investigators, students, and institutions where laboratories have been destroyed and research interrupted, to find laboratories for investigators and students so they can continue their research until their laboratories are operational.

Dr. Sassaman's next topic was re-engineering the NIEHS Core Centers Program. At the end of August, Center Directors spent a day discussing how the Centers could contribute to the Institute. At the February 2005 Council meeting a report was presented on the recommendations by the P30 Centers Assessment Committee. The following were identified in that report: defining the future directions for the Centers program, enhancing flexibility, increasing funds for pilot projects, measuring/assessing the impact of the science on public and human health as part of the review, and redefining the vision for the Community Outreach and Education Program (COEP). In response to the recommendations, we looked at the mission of the program in order to clarify and redefine its mission. We began by ensuring the program goals are in alignment with the goals of the Institute. The major changes of the new Center structure will focus on increasing flexibility, including a Health Sciences Facility Core which will provide services and expertise to conduct clinical environmental health research, providing career development that will encompass support for new young investigators, and mentoring and cross training in basic and clinical sciences. We will also change how the Centers are reviewed and assessed. The initial review will be conducted by the EHS review committee with the addition of ad hoc reviewers, without site visits. The review criteria will now include an assessment of the impact of the science supported by the Centers.

Council-Initiated Discussion

Council asked for clarification of the monies that would be allocated to the optional COEP. An additional \$100,000 will be given to the Center. Council also inquired on how the Centers were

going to entice clinicians to be a part of the research effort. The Health Sciences Facility Core will be in place to do clinical and public health research and should attract clinical researchers. Discussion also centered on how one would adequately do an assessment of the impact of the science. This is a real challenge and many approaches to looking at impact will be evaluated.

VII. Concept Clearance - Specialized Centers of Clinically Oriented Research of Environmentally Influenced Diseases (SCCORED) - Dr. Claudia Thompson (Attachment 3)

Dr. Thompson presented to the Council the concept proposal for SCCORED. She acknowledged the Integrated Medicine Initiative Committee whose members consist of, Drs. Janice Allen, David Balshaw, Kimberly Gray, Gerald Heindel, Cindy Lawler, Kimberly McAllister, Jerry Phelps, and Claudia Thompson, who developed this Concept Proposal.

Currently there are nine Center programs; why a new Center program? The SCCORED Centers will complement the infrastructure of the current Centers and is an excellent mechanism to address complex research questions. A P50 Specialized Center is proposed which will support the full range of basic and clinical research, whose activities will have a multidisciplinary approach to specific diseases or biomedical problems, and will serve as a regional or national resource for special research. The components of the Center are the following: interdisciplinary research projects, facility cores, pilot projects, training, and translational activities. The research to be supported will be basic (mechanism oriented), clinical (patient oriented), and epidemiological (population based). The outcomes from these interactions should result in improved clinical and public health practices through advances in prevention, diagnosis, and treatment of specific environmentally influenced diseases.

The proposed time line is as follows: release of RFA in November/December 2005, receipt of application October/November 2006, and Council review and awards May 2007.

Council-Initiated Discussion

Council was pleased with the integrated approaches to linking the laboratory either to population or to the bedside. There was concern that as the program develops the Centers will have a tendency to focus more on disease and disease outcomes and to allow the molecular biology and technology to focus on disease rather than fully integrating the environmental health sciences.

Council made a number of suggestions.

1. Applicants need to understand what is meant by an integrative approach before submitting their applications.
2. Policy, law and prevention should also be included as part of the clinical outcomes when looking at translational impact.
3. SCCORED should be replaced with another acronym that is unique to NIEHS to prevent confusion between NIEHS and other institutes.

Clarification was given on the physical environment in relation to translation. It was noted that the physical environment is important if it's linked to basic biology as it relates to the development and progression of disease.

Council inquired if the Specialized Centers of Clinically Oriented Research of Environmentally Influenced Diseases would be renewed after the first five years. The program will sunset in 10 years and will be evaluated. The program could be renewed but in directions that allow other pathways of development.

A motion was made and seconded for approval of the Concept Proposal which was unanimously approved.

CLOSED PORTION OF THE MEETING

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.

VIII. CONSIDERATION OF APPLICATIONS

The Council considered 322 applications requesting \$73,150,206 direct cost. The Council recommended 179 applications with the total direct cost of \$46,109,135.

ADJOURNMENT OF THE NAEHS COUNCIL

The meeting was adjourned at 4:00 p.m. on September 13, 2005.

Attachments

1. [Roster of the National Advisory Environmental Health Science Council](#)
2. [Updates of Strategic Plan and Benchmarking](#) (PowerPoint presentation)
3. [Concept Clearance - Specialized Centers of Clinically Oriented Research on Environmentally Influenced Diseases](#) (MS Word)

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
Division of Extramural Research and Training
Integrated Medicine Initiative Committee

NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL
September 13, 2005

Concept Clearance
For
Specialized Centers of Clinically-Oriented Research on Environmentally-influenced
Diseases (SCCORED)

Introduction:

Environmental health sciences research has traditionally been organized into broad areas of scientific interest with limited integration across scientific disciplines. This approach is reflective in the NIEHS grants portfolio, which supports diverse research activities of basic in vitro and animal research, population-based studies and only a limited number of patient-oriented studies that focus on the effects of environmental stressors on biological function and disease risk. The application of technological advances to biomedical research has provided unprecedented insight into the dynamic and complex nature of biological systems. With the appreciation that environmental factors contribute to most complex diseases, many of the tools are now available to embark in a new direction that focuses on integrating basic environmental health research with patient-oriented and population-based studies. The overarching goals of this program are to (1) accelerate basic scientific discoveries in environmental health sciences to understand human disease; and (2) move this knowledge into clinical application to ultimately improve public health.

NIEHS recognizes that to accomplish this, two types of research need to converge. First, the research team needs to focus on a type of human disease that is likely to be caused or influenced by an environmental exposure. Second, a team of basic, clinical and public health scientists need to work together to use environmental health sciences to understand a human disease that will ultimately improve human health. Thus we propose a new centers program to address the complex etiology and multiple factors involved in disease pathogenesis by bringing together clinical researchers working in partnership with basic science researchers from diverse fields and creating an infrastructure to support collaborative research in environmental health.

The goal of collaborative research between basic and clinical scientists is not unique to this new centers program. To a limited extent many of NIEHS's larger programs such as the Centers for Children's Environmental Health and Disease Prevention Research, the Centers for Population Health and Health Disparities, and the Collaborative Centers for Parkinson's Disease Environmental Research have moved in this direction by requiring basic and human-based components and synergy between them. The program being proposed, however, will directly respond to increased requests from the public and from Congress to shorten the time to clinical application of important basic research. This new centers program unlike others supported by NIEHS will place a much greater emphasis on broadening the focus of investigations to directly

improve human health. NIEHS believes that the intellectual and technological capacity is available to create new interdisciplinary research centers that specifically focus on complex human diseases or disorders where there is evidence or a strong rationale for the involvement of environmental factors in its etiology or phenotypic expression. These interactions should result in improved clinical and public health practices through advances in prevention, diagnosis and treatment of specific environmentally-influenced diseases.

Research Goals and Scope:

Historically, the research supported by NIEHS has emphasized a mechanistic understanding of the toxicological effects of environmental agents on biological processes. Consequently, there has been an under representation of clinically-oriented research in the environmental health sciences. The objective of this initiative is to develop a new specialized centers program that will foster scientific collaboration between basic (mechanism oriented), clinical (patient-oriented) and population-based researchers. The ultimate goal for creating these centers is to accelerate the application of knowledge derived from basic research into the clinical setting in order to improve human health in those areas where environmental factors are known or expected to influence the development or progression of disease. This centers program is expected to result in the development and application of novel approaches for the diagnosis, prevention, and treatment/intervention of environmentally-related diseases or disorders that will impact clinical or public health practice. With the creation of specialized centers that will be operating within an intervention/prevention framework, three broad themes will be intertwined to meet the goals of these centers:

- Understanding the etiology and pathogenesis of complex human diseases that are influenced by environmental factors
- Using exposure to understand the interplay between genetic and environmental factors in the etiology and progression of complex human diseases
- Applying available state-of-the-art technologies and methods to improve human health

It is envisioned that these new specialized centers will create teams that embody the basic, clinical, epidemiological, computational and engineering perspectives to focus on a disease with a clear environmental component. These centers will have a strong focus on translational research which has been defined by NIH as studies at the interface of the bench and bedside and/or community. Information flow at these interfaces is bi-directional, requiring close interaction between clinical and bench scientists to study human diseases. Mechanistic clinical studies using clinical specimens should contribute to a fuller understanding of the diseases, their etiology, pathophysiology, pathogenesis, diagnosis, and treatment. Examples of such mechanistic clinical research include:

- Identifying cellular and molecular “patterns” of disease through the understanding of interactions among multiple pathways, molecules and cell types
- Assessing the clinical implications of these patterns for disease susceptibility, development or progression and therapeutic intervention

- Conducting studies in humans that may have direct diagnostic or therapeutic application, e.g., genetic polymorphisms that relate to disease susceptibility, clinical outcome, or assessing the clinical effectiveness of a therapeutic intervention
- Screening for molecular abnormalities that relate to particular stages or manifestations of the disease
- Identifying molecular and cellular targets for novel therapies

One of the critical components of the proposed new specialized centers that set them apart from other NIH Centers programs will be their focus on the role of environment stressors in the etiology, pathogenesis and prognosis of human diseases and disorders. The consideration of environmental factors within the interdisciplinary framework of the center can be developed at multiple levels. For example:

- Environmental agents may be used as probes to dissect critical pathway components that lead to, modulate or augment the progression or risk of disease. These environmental probes would be useful to assist in developing novel therapeutic/diagnostic tools.
- Well characterized exposed populations could be utilized to identify factors that lead to variation in an individual's susceptibility to disease. These markers of disease susceptibility could then be further validated within a clinical research environment to assess the functional relevance of gene-environment interactions as it contributes to the development and progression of human disease.
- Comparative genomic, proteomic or metabolomic studies across multiple species in parallel with human studies could be conducted where exposure to environmental agents is used to facilitate the discovery of basic mechanisms of disease.
- Application of "omics" across species in parallel with human studies could be conducted to develop biomarkers of exposure or disease disposition, onset, severity or progression.
- Environmental agents may be used as tools to understand perturbations in normal cell physiology to directly link exposure to disease. This could lead to the identification and validation of biomarkers and their application as prognostic indicators of human diseases as well as therapeutic efficacy.

Many technological and methodological advances have brought forth tools that should stimulate and foster integrated approaches to achieve the goals of this centers program. Some of these include:

- the sequencing of the human genome as well as the genomes for other model organisms,
- the identification of single nucleotide polymorphisms in environmentally responsive genes and the development of haplotype maps
- the creation of genetically modified mice that mimic human conditions/disease
- the creation of suites of gene knock-outs in model organisms
- well-characterized clinical and population-based biological samples
- the development of genomic, transcriptomic, proteomic, epigenetic and metabolomic approaches and associated bioinformatic tools
- the development of imaging technologies, biosensors and nanomaterials

Mechanism and Justification:

A number of resources are available to provide guidance in developing a research centers program that promotes clinical application of environmental health sciences. The recent Institute of Medicine (IOM) Centers evaluation report encourages development of centers when the criteria focus on: 1) the importance of the problem to be addressed by the program, specifically the need for shared resources; 2) the need to develop a highly visible critical mass of multidisciplinary research in a particular area; and 3) the need to increase the number of researchers working in a particular field. The IOM report also states that the need for strategic focus, interdisciplinary interaction, and the translation of scientific knowledge into clinical or public health practice are further justifications for the existence of a Center programs. The NIEHS currently supports a Core Centers Program (P30) which provides facility infrastructure to build capacity in environmental health sciences research and to stimulate multidisciplinary collaborations. However, since the NIEHS Core Centers Program's inception, the field of environmental health sciences has changed dramatically. NIEHS therefore recently underwent an evaluation of the Centers Program to assess the success of these programs and examine the future need of Centers to meet the challenges of the field of environmental health sciences. One of the recommendations of the evaluation committee was to encourage the growth of specialized and comprehensive centers charged "to carry out extensive translational activities". It was suggested that these comprehensive centers should focus on effectively translating basic research on environmental health science discoveries (e.g., clinical research, biomarker research, molecular epidemiology) into clinical medicine and public health practice.

Based upon the recommendations of the NIEHS Centers Evaluation and the list of criteria suggested by the IOM report, the NIEHS is bringing forth a plan to develop a new specialized centers program that utilizes the NIH P50 mechanism. This mechanism supports research projects as well as facility cores. The Centers must utilize a multi/inter-disciplinary approach to a disease-targeted theme and the individual projects must uniquely contribute to the overall theme. These Centers programs should encourage the application of new scientific findings to clinical problems or public health issues.

In summary it is believed that the resources and intellectual capacity are in place to create a new specialized centers program that focuses on integrating basic environmental health research with patient-oriented and population-based studies to accelerate basic scientific discoveries into the clinical setting to improve human health through affecting clinical or public health practice.