

**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 26, 2005**

The National Advisory Environmental Health Sciences Council was convened for its one hundred twelfth regular meeting at 8:30 a.m. on February 14, 2005, in Building 31, Conference Room 6C6, National Institutes of Health, Bethesda, MD. Dr. Kenneth Olden presided as Chair.

The National Advisory Environmental Health Sciences Council was convened for its one hundred fifteenth regular meeting at 8:30 a.m. on May 26, 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 May 26, 2005, from 8:30 a.m. to 2:00 p.m. in accordance with the provisions of Public Law 92-463. The meeting was closed to the public on May 26, 2005, from 2:00 p.m. to 4:00 p.m. for consideration of grant applications. Notice of the meeting was published in the Federal Register.

Members Present:

Teresa Bowers, Ph.D.
Deborah Brooks
Kathleen Dixon, Ph.D.
Elaine Faustman, Ph.D.
Bruce Freeman, Ph.D.
Bernard Goldstein, M.D., Ph.D.
George Gray, Ph.D.
Lisa Greenhill, MPA
Daniel Liebler, Ph.D.
David Losee, J.D.
Martin Phillbert, Ph.D
Peter Spencer, Ph.D.
Peter Thorne, Ph.D.
James Townsel, Ph.D.

Members Absent

Douglas Benevento, J.D.
Charli Coon, J.D.
William Owen, Jr. M.D.
Frank Talamantes, Ph.D.

Ex Officio Members Absent

COL James S. Neville

Liaison Members Present

Olivia Harris - Alternate. (National Center for Environmental Health, ATSDR, CDC)

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

Kendall Wallace, Ph.D. (Society of Toxicology)

Liaison Members Absent:

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

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

NIEHS Staff

Kathy Ahlmark

Janice B. Allen, Ph.D.

Beth Anderson

Lisa Archer

David Balshaw, Ph.D.

Amber Barnes

Martha Barnes

Linda Bass, Ph.D.

Sharon Beard

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.

Pamela Evans

Richard Freed

Lerlita Garcia

Kimberly Gray, Ph.D.

Jerrold Heindel, Ph.D.

Michael Humble, Ph.D.

Ethel Jackson, D.D.S.

Laurie Johnson

Michealan Jones

Robin Mackar
Marian Johnson-Thompson, Ph.D.
Annette Kirshner, Ph.D.
Dennis Lang, Ph.D.
Cindy Lawler, Ph.D.
Elizabeth Maull, Ph.D.
Carolyn Mason
J. Patrick Mastin, Ph.D.
Kimberly McAllister, Ph.D.
Rose Anne McGee
Kim Minneman
Teresa Nesbitt, DVM, Ph.D.
Liam O'Fallon
Michelle Owens
Theodore Outwater
Jerry Phelps
Christopher Portier, Ph.D.
Leslie Reinlib, Ph.D.
Margarita Roque
Anne P. Sassaman, Ph.D.
Carol Shreffler, Ph.D.
Shobha Srinivasan, Ph.D.
William Suk, Ph.D.
Claudia Thompson, 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 fiftteenth regular meeting of the National Advisory Environmental Health Sciences Council to order. Dr. Schwartz, in his opening remarks, expressed how honored he felt to step into the leadership of NIEHS and to work with the scientific community and NIEHS to build successful programs and to create a new vision for NIEHS. He then introduced the new members of Council: Drs. Kathleen Dixon, Bruce Freeman, Daniel Liebler, Ms. Lisa Greenhill and Dr. Kendall Wallace, a liaison member representing the

Society of Toxicology. 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.

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 14-15, 2005 meeting were approved as written.

FUTURE COUNCIL MEETING DATES

The following dates for September and February were confirmed

September 15/16, 2005, NIEHS, Thursday Friday

February 16/17, 2006, NIEHS, Thursday Friday

June 12, 2006, NIEHS, Thursday Friday

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

Dr. Schwartz began his presentation with a brief overview affirming that the field of environmental health sciences is like no other. The field is not limited by a biological system, a disease process, or an organ system. In fact, the field of environmental health sciences represents the critical link between exposure and disease for many other fields of biomedical research. The NIEHS, because of its focus and concentrated expertise, is uniquely poised to develop sensitive preclinical markers of exposure and biological response; develop strategies to prevent disease in exposed and biologically responsive individuals and populations; establish population-based cohorts to understand the impact of environmental exposure on human health; understand how environmental exposure affects the course and prognosis of a medical condition; and stimulate dialogue to advance our understanding of environmental health policy and ethical issues of environmental concern.

Dr. Schwartz then stated that as we work to move NIEHS forward, it is important that we consider how the research can have the greatest impact on public health. He identified the vision for NIEHS which will be to improve human health by elucidating a complex relationship between endogenous and exogenous risks within populations and affected individuals, how environmental exposures affect human biology, and how this knowledge can be used to reduce morbidity and extend longevity. Fundamental to this vision is an emphasis on human health and disease. He then gave examples of previous research areas supported by the NIEHS that have had a profound effect on human health.

He further mentioned that the following approaches and values will support the vision. NIEHS will be supporting the very best science that will have the greatest impact on human health. NIEHS will integrate environmental sciences with related disciplines (basic science, computational biology, medicine, and public health) and focus on relevant disease processes. In order to prepare for the future, there will be an enhancement of research opportunities, recruitment, training, and support for the next generation of scientists. There will be support for new scientific approaches which are likely to impact the field of environmental sciences. NIEHS will partner for greater impact and create strategic alliances.

Dr. Schwartz then presented the NIEHS' history of past assessments and outside reviews of the research directions and priorities, which aided in setting priorities, readjusting the course of scientific inquiry, and establishing new goals. He noted that NIEHS has benefited greatly from the input of the nation's top scientists and experts in environmental health sciences in this process. He also noted that it is timely that NIEHS will be embarking on the development of a strategic plan to consider future programmatic development. Given the anticipated limited resources for the foreseeable future, it is crucial that priorities are established and a plan is developed to support the best science that will have the greatest impact on human health.

Dr. Schwartz emphasized that the scientific community and interested non-scientist stakeholders will be included in the process of strategic planning that will take place over the next year. The group will include a broad array of environmental health scientist engaged in toxicology, medicine, epidemiology, public health, basic biology, and genetics. The time line is as follows:

1. Requests for information will be solicited through the Federal Register and NIEHS website.

Key questions are as follows:

- o What are the disease processes and public health concerns that are relevant to environmental sciences?
 - o How can environmental sciences be used to understand how biological systems work, why some individuals are more susceptible to disease, or why individuals with the same disease have very different clinical outcomes?
 - o What are the major opportunities and challenges in global environmental health?
 - o What are the critical exposures that need further investigation?
 - o What are the mission-critical needs in training the next generation of scientists in environmental health?
 - o What technology or structural changes are needed to fundamentally advance environmental health science?
2. A local strategic working group will be established to plan and oversee the process.
 3. A Strategic Planning Group of approximately 100 scientists and stakeholders will meet in September 2005 and produce a brief document that outlines the goals and objectives to warrant the greatest scientific and programmatic attention over the next several years.

4. The draft document will be vetted for public comment on the NIEHS website and the Federal Register, and through the NIEHS Advisory Council before a final document is compiled.
5. The final document should be completed in early 2006.

The goal will be to establish priorities and develop a plan that will have the greatest impact on human health over the next five years.

Dr. Schwartz concluded his presentation with the statement, "We have unparalleled opportunities to achieve groundbreaking advances in science and to translate these advances into measurable improvements in human health."

V. Vision for the Future and Role and Operation of Council Dr. Schwartz and Council

Following the Director's report, the Council engaged in a discussion centered on the vision Dr. Schwartz had proposed for NIEHS.

The discussion began with the need to build new constituencies. Council expressed the need to reach out to other organizations, such as the legal community (not just the existing regulators, but the law schools). It is important that the legal community be informed of environmental science issues, so that timely and appropriate legal policy can be put into place. In this regard, council suggested consideration of support of a program in Policy Ethics Law at it relates to environmental sciences. One issue would be how to develop policy for vulnerable populations with an environmental risk that is not faced by the rest of the population.

Continue to work with Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and Occupational Safety and Health Administration (OSHA), all of which are struggling with the same issues as NIEHS making sure that the legal profession, especially those working at these agencies, works for translation into policy. Also, we want to integrate the vision of National Toxicology Program (NTP) into the extramural activities at NIEHS so that the vision is seamless.

The Council expressed concern about the human exposure studies that are before Congress. The congressional action could be a setback for future studies of this type. It is very important to clearly communicate the importance, the vision, expected outcomes, the opportunities and the potential impact of the future studies. They emphasized the need for clear and consistent communication. Dr. Schwartz asked Council to work with him in educating the public and the legislature as to why these studies are important.

Council commended Dr. Schwartz on moving into new and bold directions and maximizing the impact of the Institute. They asked him if thought had been given to cost; balancing the portfolio; balancing big science versus small-scale serendipity, and assessing the price associated with the perception of disenfranchisement as programs shrink and others expand.

Dr. Schwartz acknowledged that we will not be able to appease everyone; however, tough choices will have to be made. He hopes, with the help of the extramural staff, to balance the

science portfolio and choose the best of "big" and investigator-initiated science. It is understood that we cannot support an entitlement program, but only a high quality peer-reviewed program. NIEHS has been entrusted with public funds, and therefore has the responsibility of funding the very best research. There will be problems with this philosophy and we will have to deal with the problems. It is his hope that Council will help articulate the need for taking on this philosophy.

It was noted by Council that transparency for the advocacy community is incredibly important. It should be made clear that decisions may or may not be what they want, but they will have a voice in the process. Also, the public health, the community-based, and the global environmental issues that we will be dealing with will place us in the communities and the populations that are uniquely at risk. It is important to understand these communities.

Dr. Schwartz commented that one of the groups he proposes to convene in the fall will include individuals from the advocacy community as a way of getting buy-in, participation, and an understanding of the process that will identify the goals and priorities over the next several years.

Council commented that when formulating the Strategic Plan we need to look at the role NIEHS can play to understand human variability. Some of the questions that need to be thought about are, why do some people respond to the disease/environmental exposure and others do not? Why do some have good outcomes following the development of a disease and others do not? What makes this Institute unique? Understanding environmental exposures is another way of understanding biology.

As a segue to Dr. Wilson's remarks, Dr. Schwartz announced that Dr. Wilson has agreed to stay on as Deputy Director, spoke of his many outstanding attributes, and indicated that Dr. Wilson has conceptualized the development phase of what NIEHS is proposing to do: integrate basic science into pathophysiologic and disease processes in a meaningful way.

Dr. Wilson began the discussion by commenting on the need to discuss better ways to maximize efficiency toward meeting the goal of impacting human health and disease and how to integrate research across various disease categories. How do we achieve an integrated program so that we make use of the basic science resources that we already have in place and then develop new translational approaches and resources for the clinically-focused research that we would need in order to have an impact?

Over the past several years we have been discussing how to most effectively and efficiently impact human health and disease. We wondered about the idea of identifying certain disease categories and then exploring how an integrated approach through basic science (pre-translational science) and translational science might be accomplished in combination with clinical research, epidemiology, community outreach, and policy development. The question is how do we integrate basic science across the various disease categories. Is this the most appropriate rationale for setting priorities so that we are able to support the research and leverage it with other NIH institutes and other parts of the community? NIEHS needs to determine whether this is the appropriate model and if so how can we achieve the objectives.

Normally we look at what we think might cause the disease, and most often have not found the cause of the disease. The alternative or complementary approach is to look at the disease, find out what the environmental component is and then go after those factors to understand pathogenesis, prevention, and treatment. This is a Sea change” (big change) in thinking which will bring some resistance, but can be accomplished in time.

Nevertheless, the scientific community has other drivers for their research beside human health and disease that NIH is mandated to address. We need to come up with a philosophical framework that achieves this broader attack on human health and disease, but at the same time incorporates the needs of the academic community in terms of what they are dealing with on a day-to-day basis. The culture of how we do research at NIH and across the academic community would have to gradually change.

Dr. Schwartz concluded the discussion by commenting that the Institute will continue to support fundamental research (basic research) as it relates to environmental sciences that is not necessarily integrated into the more clinically, pathogenically driven or public health related. However, it is very important that we look to create a much more integrated approach to problems that we know are fundamentally based in environmental exposures, thereby creating a greater impact.

VI. Concept Clearances

Nanoscale Science and Environmental Health Dr. Sally Tinkle (Att. 1)

Dr. Sally Tinkle presented to the Council the Concept proposal for Nanoscale Science and Environmental Health. She introduced Drs. David Balshaw, William Suk, and J. Patrick Mastin who helped in developing the Concept proposal. She began her presentation with a brief history on nanoscale science and technology, the National Nanotechnology Initiative, and the strategic plan.

The Concept proposal outlined a plan to support multidisciplinary research on environmental and biological impact of nanomaterials. Due to the projected increase in demand and production of nanomaterials it is expected there will be an increased potential for exposure that will require an understanding of the biological and societal impact of the technology and its use. Therefore, additional research will be needed to understand the relationship of dose as a mass measurement to surface area and particle number, routes of exposure, the mechanisms of cellular uptake and response, including biotransformation and biopersistence, and the relationship of the particle’s physical and chemical characteristics to the biological response.

In addition to research on the biological impact of nanomaterials exposure, nanoscale science creates the potential to develop multifunctional platforms that can be use in vitro and in vivo to report toxicological parameters such as internalized dose, tissue distribution, and biological response. Nanoscale probes that facilitate research on disease etiology, biomarkers of exposure and disease, and toxin detection and elimination support the NIEHS mission to understand the environment-disease interaction and may be developed within this context.

Dr. Tinkle concluded by describing the solicitation mechanisms, which will include one or more initiatives that utilize Request for Applications (RFAs) and Program announcements (PAs) to encourage submission of R21 applications (development of potential research programs) or R01 applications (building upon existing data and programs). Multidisciplinary research teams will be encouraged and collaborative research efforts may require the use of the U01 and U19 mechanisms. Interagency agreements will be utilized as appropriate to support NIEHS research goals.

Council-Initiated Discussion

Dr. Tinkle's presentation generated questions centered on clarifying the roles and responsibilities in the Nanomedicine Roadmap initiative and the NIEHS initiative. In terms of manufactured nanomaterials, the discussion was in reference to occupational exposure. Council also encouraged the institute to view the positive aspects of nanotechnology in environmental health development and use of nanotechnology in basic research and exposure assessment measurements.

A motion was made and seconded for approval of the Concept. Council unanimously approved the Concept proposal.

Integrative Environmental Health Research Dr. J. Patrick Mastin (Att. 2)

Dr. Mastin began his presentation by reemphasizing the need to employ a research approach that involves researchers from many disciplines, an integrated environmental health approach to fully understand and address human diseases. Therefore, it is proposed that funds be targeted to achieve this integrative approach through the portfolios already in existence. Some of the obstacles will be the culture (researchers like to keep doing what they are familiar with), researchers are hesitant to invest their intellectual capital or divert funds from what is already a productive endeavor into a new field, and applications of this type are not reviewed favorably at the Center for Scientific Review (CSR). Therefore, an Integrative Environmental Health Research Program is proposed to provide an incentive by setting aside funds, instituting special review criteria, and a special review panel for this type of research.

In order to facilitate the development of these kinds of integrative research efforts, it is proposed that one or more initiatives be developed over a period of several years, which will provide support to establish or expand multidisciplinary collaborations between basic and clinical researchers. Applications in response to these initiatives would include basic and clinical research components, would have to propose research on an environmentally related disease, disease process, or dysfunction and would involve an environmental exposure. Mechanisms of support could include R03 (planning grants), R21 (developmental grants) for investigators who are beginning to develop the necessary collaborations and R01 for teams that are further along in their collaborative efforts or for targeting certain areas for collaborations. Progress and success could be monitored by grantees meetings and formal evaluations. Dr. Mastin concluded his presentation by calling on Dr. Liebler and Ms. Brooks to begin the Council discussion.

Council-Initiated Discussion

Council thought the Concept proposal was great for enhancing the vision of NIEHS, but the challenges will be to bring relevant individuals together. They also felt planning needed to take place on the type of collaborative efforts sought. Staff should look at what type of teams will be the most productive and provide the most positive outcomes. Before grantees are sought, thought should be given to how the coordination will deliver the outcomes wished to be achieved and not those that are linked under a common topic or area of interest. Build into the program, to increase efficiency and effectiveness, structured timelines, specific and scientific milestones, and funding contingent on reaching the prescribed milestones. Concern was expressed that there will be only one principal investigator and how will co-investigators get recognition at their universities? Will it be possible to have more than one principal investigator? Council felt the biggest challenge will be size and scope of the collaborations and selecting the environmental and pathogenic mechanism that leads to a disease; this should not be just another big or targeted program.

A motion was made and seconded for approval of the Concept. Council unanimously approved the Concept proposal.

Outstanding New Environmental Health Scientist Award ' Dr. J. Patrick Mastin (Att. 3)

Dr. Mastin began his presentation by updating Council on the training and fellowship programs NIEHS currently supports. To augment the current career development mechanisms and assure a cadre of productive environmental health science investigators for the future, NIEHS is proposing to support a program of R01 research grants intended for the first-time R01 applicants. Incentives are provided by setting aside funds, creating special review criteria, and instituting a special review panel for this type of R01 mechanism.

Through this announcement NIEHS will be seeking outstanding, highly creative and promising junior scientists who intend to make a longterm career commitment to research in environmental health sciences. These young scientists will bring innovative, ground-breaking research initiatives and thinking to bear on the problems of environmental exposures and human biology, human pathophysiology and human disease.

This R01 grant application will have four distinguishing features from the typical R01 application. First, less emphasis will be placed on preliminary data; however, emphasis will be on previous research experience and achievements, applicant's future goals and objectives and plans for enhancing their careers; second, applicants will require mentorship and scientific feedback on their research, and institutional commitment through continued faculty development; third, departmental commitment is required in the form of dedicated lab space and letters of support from the departmental chair; and fourth, a budget which includes equipment, resource development, career enhancement activities, and travel.

Institutions will be limited in the number of junior faculty who may apply; thereby, only selected investigators will be able to apply.

In conclusion, NIEHS hopes to provide a competitive award that will target and attract highly qualified new investigators to careers in environmental health science.

Council-Initiated Discussion

Council reiterated the need to target outstanding junior scientists and enhance their career development with supervised mentorship and start-up funds. In the long-term NIEHS will have an excellent cadre of innovative, productive, environmental health science investigators.

A motion was made and seconded for approval of the Concept. Council unanimously approved the Concept proposal.

VII. National Toxicology Program (NTP) Today Dr. John R. Bucher

Dr. Bucher gave an overview of the NTP organization which consists of the Executive Committee (policy oversight) and the NTP Board of Scientific Counselors (external science oversight and peer review) who both report to the Director NIEHS. The Director NIEHS interacts with the National Center for Toxicological Research (NCTR), and the National Institute of Occupational Safety and Health (NIOSH). He noted that the scientific and technical staff are from NIH/NIEHS (75), FDA/NCTR (33), and CDC/NIOSH (12).

Highlights on the following activities were given: the Dioxin TEF Evaluation, Herbal Medicines, Cardiotoxicity, Imaging Techniques, Safe Water, Hexavalent Chromium, Polybrominated Diphenyl Ethers, Electromagnetic/Radiofrequency Radiation, the Nanotechnology Safety Initiative, Gene Therapies, Complex Occupational Exposures, Endocrine Disruptor Initiative, NTP Center for Phototoxicology, Transgenic Animals in Cancer Testing, Transgenic Mouse Models, Toxicogenomic Research, Mechanism-Based Mathematical Modeling, Center for the Evaluation of Risks to Human Reproduction, Report on Carcinogens, NTP Interagency Center for the Evaluation of Alternative Toxicological Methods, and the NTP Research Databases.

He informed Council that NTP is mounting an effort to put all of its research data into an Oracle-based database accessible for searching from the Internet. Therefore, within the year, individuals will be able to search any of the endpoints that have come out of the NTP testing program.

Dr. Bucher pointed out the expectations for the program. NTP will continue to provide basic toxicology information for public health protection; increase the emphasis on understanding and explaining exposure-response relationships; continue to integrate new data-rich technologies such as genomics and proteomics; develop new methodologies for toxicological assessments and not only develop those new methodologies, but work with the regulatory agencies to provide guidance for the proper utilization for the new type of information in hazardous identification and characterization.

He concluded by stating that NTP today is leading the nation in research aimed at the prevention of environmental causes of disease; providing the science that supports public health decisions regarding environmental exposures; partnering with as many stakeholders as possible to improve risk characterization and assessment; and developing the tools to move toxicology and risk assessment forward to meet the demands of the twenty-first century.

Council-Initiated Discussion

Council questioned if the NTP will incorporate the NTP data into the Chemical Effects in Biological Systems (CEBS) database or will these remain as two separate databases. It was stated that these should be eventually one database.

Also Council wanted to know if pharmacological agents tested by NTP are mandated by FDA. At the moment nothing is mandated, the choice of what to study, and how it's studied is made by NTP.

Council thanked Dr. Bucher for an informative presentation.

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 386 applications requesting \$92,873,679 in total direct cost. The Council recommended 217 applications with the total direct cost of \$56,933,511.

ADJOURNMENT OF THE NAEHS COUNCIL

The meeting was adjourned at 4:00 p.m. on May 26, 2005.

Attachments

1. [Nanoscale Science and Environmental Health](#)
2. [Integrative Environmental Health Research](#)
3. [Outstanding New Environmental Health Scientist Award](#)

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Division of Extramural Research and Training
Center for Risk and Integrated Science
Cellular, Organs, and Systems Pathobiology Branch

NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL

May 26, 2005

Concept Clearance
for

Nanoscale Science and Environmental Health

Nanoscale science and technology involve the imaging, measuring, modeling and manipulation of matter on the scale of 1 to 100 nanometers - a scale at which novel physical, chemical and biological properties enable novel applications. Nanoscale materials and devices frequently provide increased sensitivity and selectivity, improved electrical and optical properties, and permit development of multifunctional sensor platforms. Nanoscale products are useful in the health sciences for drug delivery, tissue engineering, biological and environmental sensor technology, and environmental remediation. Consumer products containing nanoscale materials, such as sunscreens and stain resistant fabrics, are commercially available, and by 2010, the nanoscale materials, tools and devices industry is projected to exceed \$10 billion.

At the direction of the President, the Nanoscale Science, Engineering and Technology (NSET) Subcommittee developed the National Nanotechnology Initiative (NNI) to coordinate and support responsible development of nanomaterials and devices. The NNI Strategic Plan organizes research and development into seven Program Component Areas (PCA):

1. Fundamental Nanoscale Phenomena and Processes, 2. Nanomaterials, 3. Nanoscale devices and systems, 4. Instrumentation Research, Metrology, Standards, 5. Nanomanufacturing, 6. Major research facilities and instrumentation acquisition, and 7. Societal Dimensions.

The NIH participated in the development of the Strategic Plan, and the nanomedicine component of the NIH Roadmap and the nanoscale materials and devices component of the NIH Bioengineering Consortium (BECON) are consistent with activities described in PCA 1, 2, and 3. Through these two entities, NIH supports research on the physical and chemical properties of intracellular molecules and nanomachinery and use of this information to develop new nanotechnologies, devices and hybrid structures that prevent and treat disease.

The NIEHS mission, unique among NIH ICs, aligns with requirements in the Strategic Plan to understand the environmental health and safety impact of nanomaterials and products, including potential adverse health effects, to develop devices that measure exposure and the health consequence of exposure, to explore the ethical, legal, social and economic implications, and to develop public outreach and education programs. These activities are consistent with PCA 3 and 7 and complimentary to the NIH Nanomedicine Roadmap initiative.

This concept proposal outlines a plan to support multi-disciplinary research on the environmental and biological impact of nanomaterials and strengthens NIEHS activities in the National Nanotechnology Initiative, NIH Nanomedicine Roadmap, and in the NIH Bioengineering Consortium. It is collaborative with the Nanotoxicology Program developed by the National Toxicology Program/NIEHS.

Research Goals and Scope

The projected increase in nanomaterial demand and production will be accompanied by increased opportunity for exposure and will require an understanding of the societal impact of the technology and its use. Recent research on the biological impact of nanomaterials indicates that the novel physical, chemical and biological properties are a function of composition, a large surface area to mass ratio, crystalline structure, shape, surface chemistry, stability, and potential for self assembly. Several medical sensors and drug delivery systems have demonstrated biological compatibility, while other materials perturb homeostasis or cause frank disease. Early research has demonstrated that nanomaterials may impair pulmonary clearance, skew the immune response or promote development of pulmonary fibrosis and foreign body granulomas. Additional research will be needed to understand the relationship of dose as a mass measurement to surface area and particle number, routes of exposure, the mechanisms of cellular uptake and response, including biotransformation and biopersistence, and the relationship of the particle's physical and chemical characteristics to the biological response.

In addition to research on the biological impact of nanomaterials exposure, nanoscale science creates the potential to develop multifunctional platforms that can be used *in vitro* and *in vivo* to report toxicological parameters such as internalized dose, tissue distribution, and biological response. Nanoscale probes that facilitate research on disease etiology, biomarkers of exposure and disease, and toxin detection and elimination support the NIEHS mission to understand the environment-disease interaction and may be developed within this context.

Suggested research topics include, but are not limited to:

- Exposure and risk assessment
- Comparison of routes of exposure, magnitude of exposure, and systemic distribution
- Molecular, cellular and organ system compensatory mechanisms or toxic response
- Determinants of biological compatibility or toxicity, such as surface composition and chemistry, size and shape, biotransformation and biopersistence
- Technologies developed within the context of research addressing a specific environmentally-induced disease, including tools to support exposure or risk assessment, biologic mechanism or therapeutic intervention
- Exploration of the ethical, legal and societal impact of nanoscale materials production and use
- Education and public outreach

Mechanisms

It is anticipated that the solicitation mechanism will include one or more initiatives that utilize Requests for Applications and Program Announcements to encourage the submission of R21 applications (development of potential research programs) or R01 applications (building upon existing data and programs). Multidisciplinary research teams will be highly encouraged, and

collaborative research efforts may require use of the U01 and U19 mechanisms. Interagency agreements are highly encouraged under the National Nanotechnology Initiative and will be utilized as appropriate to support NIEHS research goals.

Because nanotoxicology is a new field, the progress and success of this program could be monitored as an increase in the number of nanotoxicology research laboratories, funded applications, and peer-reviewed manuscripts.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Division of Extramural Research and Training
Cellular, Organ, and Systems Toxicology Branch

NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL

May 26, 2005

Concept Clearance
for

Integrative Environmental Health Research

The mission of NIEHS is to support research in the understanding, detection, prevention, and intervention of environmentally related disease and disease processes. This mission has historically been accomplished in part through a diverse extramural research portfolio consisting of basic in vitro and animal research, population-based and controlled human exposure studies, and a limited number of patient-oriented studies. The ultimate goal has always been to support research that could be applied to reducing disease burden and improving public health. However, in recent years there has been increased pressure from the public and from Congress to shorten the time to clinical application of important basic research. In response, NIH included a Translational Research Initiative under the Roadmap “Re-engineering the Clinical Research Enterprise” theme. NIEHS has likewise required basic and human-based components in several of its larger programs, including 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. In addition, some program project grants have included both basic and human-based projects. However, investigator-initiated proposals, such as R01 grant applications, which constitute the largest portion of extramural support, have not sufficiently incorporated this cross-disciplinary approach, resulting in a delay in the integration of basic biology discoveries into clinical applications, and in many cases the absence of efforts to integrate basic discoveries into public health applications.

Part of the difficulty in conducting research that spans the basic-to-human research spectrum is recognition that most diseases are multi-factorial and result from the interactions among genetics, environmental exposures, lifestyle, age, exposure to infectious agents, etc. Therefore, a multidisciplinary, interdisciplinary approach is needed to address the complexity of disease processes as well as to bridge the gap between basic and clinical research.

Research Goals and Scope

The purpose of this effort is to encourage investigators to develop cross-disciplinary collaborations that will hasten the application of basic research results to improvement of public health. In addition to identifying and supporting specific collaborations, the long-term hope is that this program will begin moving investigators away from believing that such integrative approaches are noteworthy accomplishments to seeing them as the norm. While this is a goal for all NIH institutes, NIEHS is uniquely situated to take advantage of this paradigm, due to its focus on diseases that occur as a result of environmental exposures. For instance, collaborations

across the basic/clinical spectrum could lead to the development and validation of better diagnostic and screening methods (e.g., biomarkers); enhance our ability to identify environmental agents that cause human disease; facilitate the identification environmental contributors to the risk of “idiopathic” disease; help develop intervention strategies, including environmental remediations and drug therapies; and enhance the development and validation of animal models.

The remarkable evolution in technology in the last decade supports the timeliness of this effort. The use of genomic, proteomic, and metabolomic analyses, transgenic / knock out animals, RNAi technology, and genetic analysis methods (e.g., QTL, linkage analyses, and SNP analysis) make cross-species comparisons and extrapolations far easier than before. In addition, the growing evidence that many common diseases and dysfunctions, such as Parkinson’s disease, cardiovascular disease, and reproductive dysfunction, have environmental components points out a need for this type of research approach and increases confidence in its success.

Researchers are understandably cautious about investing intellectual capital in new research directions and diverting resources from already productive programs. Making funds available for this activity, over an extended period of time, will hopefully reduce these apprehensions. Some investigators will already have begun to establish these kinds of collaborations while others have only begun to consider them, so consideration needs to be given to how best to assist collaborations at the different levels of maturity. In addition, given the perception that CSR study sections are not generally favorable to multi/interdisciplinary applications it will be important to have applications from these initiatives reviewed by special emphasis panels. Some scientific obstacles, such as the development of tools for doing cross-disciplinary research, also undoubtedly exist, but we believe that by encouraging researchers from diverse areas to come together, most of these technical issues will be worked out.

Mechanisms

In order to facilitate the development of these kinds of integrative research efforts at the R01 investigator-initiated level, we propose to develop one or more initiatives over a period of several years that will provide support to establish or expand multidisciplinary collaborations between basic and clinical researchers. Applications in response to these initiatives would clearly have to include basic and clinical research components, would have to propose research on an environmentally related disease, disease process, or dysfunction, and would therefore also have to involve an environmental exposure. The mechanisms of support could include R03 planning grants or R21 developmental grants for investigators who are beginning to develop the necessary collaborations, and / or R01s for teams that are further along in their collaborative efforts. As mentioned above, part of the purpose of this effort is to stimulate investigators to think about a more integrative approach to their research, and the developmental and planning grants would ideally encourage more researchers to consider moving their research in this direction. The R01s could also be used to target certain areas where there are known opportunities for successful collaborations.

The progress and success of this program could be monitored in two ways. First, grantees meetings could be held to allow awardees to discuss their successes and obstacles in developing collaborations. Second, at the end of the initiatives, formal evaluations of, for instance, cross-

training activities, submission of co-authored papers, and /or submission of new integrated research applications, might be conducted.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Division of Extramural Research and Training
Cellular, Organ, and Systems Pathobiology Branch

NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL

May 26, 2005

Concept Clearance

For

Outstanding New Environmental Health Scientist Award

An essential element of the mission of the National Institute of Environmental Health Sciences is the support and career promotion of the future generation of exceptionally talented and creative new scientists who will further the understanding of the impact of environmental exposures on human health. The NIEHS supports a number of training and fellowship programs for pre and postdoctoral training, and mentored career development awards for junior faculty development. Primary among these are the Ruth Kirschstein National Research Service Awards for pre and postdoctoral training, the Career Development Awards for clinically trained scientists (K08 and K23), and the Mentored Quantitative Research Career Development Awards to support the career development of scientists quantitative and engineering backgrounds who wish to integrate their expertise with biomedicine. In addition, in 1999 the NIEHS instituted the Transition to Independent Positions Program to address the progression of individuals from postdoctoral positions to faculty positions. In this career development award the individual applies for the grant while still in a postdoctoral position, and the grant for start up funding is awarded at the institution where the candidate accepts the faculty position. However, even with these career development mechanisms in place, to fulfill its mission of assuring a cadre of productive environmental health science investigators for the future, NIEHS needs to initiate further imaginative programs to identify the best new biomedical investigators and facilitate their establishing vibrant, independent research programs in the environmental health sciences.

Research Goals and Scope

In order to identify outstanding junior scientists at the formative stages of their career and assist them in launching an innovative research program with a defined impact in the environmental health sciences, the NIEHS is proposing to support a program of R01 research grants intended for the first-time R01 applicant. It will be designed to be highly competitive and only a limited number will be awarded per year.

Research programs supported by this announcement seek to promote career advancement of the best, highly creative and promising junior scientists who intend to make a long-term career commitment to research in the mainstream of the environmental health sciences, and bring innovative, ground-breaking research initiatives and thinking to bear on the problems of environmental exposures and human biology, human pathophysiology and human disease.

Mechanism(s)

It is expected that one or more initiatives will be developed to facilitate the identification and support of promising new investigators.

Applicants to the RFAs will be expected to demonstrate how the proposed research will have a defined impact on the environmental health sciences and be responsive to the mission of the NIEHS, which is distinguished from that of other Institutes by its focus on research programs seeking to link the effects of environmental exposures to the cause, moderation, or prevention of a human disease or disorder. For the purposes of this announcement, applications will be expected to focus on a specific human disease, dysfunction or pathophysiological condition and propose to study a specific, relevant environmental agent.

The research grant applications in this program are distinguished from other R01 research applications in four other respects. First, although applicants are encouraged to provide preliminary data to support their proposals, less emphasis will be placed on this aspect of the applications than with other R01s. Instead, additional emphasis will be given on the applicants' previous research experience and achievements, their future career goals and objectives, and their plans for enhancing their careers.

Second, applications will also require the active participation of an advisory committee composed of senior internal and external scientists to provide mentorship and scientific feedback on the research, and require demonstrated commitment by the institution to the research program and continued faculty development of the Principal Investigator.

Third, because active support from a new investigator's department is crucial to their career development, applicants will be required to demonstrate this support in the form of dedicated lab space and letters of support from their department chairs.

Fourth, since NIEHS is proposing to make a substantial commitment to the research career of the principal investigator, it is proposed that budgets submitted in response to this program will include a separate budget specifically devoted to equipment, resource development and career enhancement activities. The budget will also include an enhanced travel budget.

Because of the special competitive nature of this program, institutions will be limited in the number of junior faculty who may apply.

The goal of this program is to provide funding opportunities that will be attractive to promising new investigators, because it will be targeted to them and because the applications will be reviewed in a special emphasis panel. By limiting the number of applicants from each institution, only select investigators will be able to apply. This will allow NIEHS to identify the top echelon of new biomedical investigators, and provide them additional start up funds to facilitate their future success. Finally, the requirement for an environmental health focus will give NIEHS a competitive edge in the search for talented researchers.