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 10-11, 2001

The National Advisory Environmental Health Sciences Council was convened for its one hundred fourth regular meeting on September 10, 2001, at 8:30 a.m., in Rodbell Auditorium, Building 101, National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, North Carolina. The meeting was open to the public from 8:30 a.m. until 5:00 p.m. and on September 11 from 8:00 a.m. until 9:00 a.m. The meeting was closed for consideration of grant applications on September 11 from 9:00 a.m. until 10:30 a.m. Dr. Kenneth Olden presided as Chair on September 10-11, 2001.

Members Present:

Daniel Baden, Ph.D.
Nancy Chuda
Joan Cranmer, Ph.D.
Deeohn Ferris, J.D.
George Friedman-Jimenez, M.D.
Michael Gallo, Ph.D.
Barbara S. Hulka, M.D., M.P.H.
Philip M. Iannaccone, M.D., Ph.D.
R. Michael McClain, Ph.D
Robert D. Wells, Ph.D.
Martyn T. Smith, Ph.D.

Members Absent:

Noreen Clark, Ph.D.
Dale Eastman
Frederick P. Guengerich, Ph.D.
Michael Karin, Ph.D.
Daniel W. Nebert, M.D.
Hon. Harriett M. Wieder

Ex Officio Members Present:

Kelley Brix, Ph.D.

Liaison Members Present:

Daniel Acosta Jr., Ph.D.
Michael Galvin, Ph.D.

Members of the Public Present:

James Chuda
Larry Marnett, Ph.D.

Federal Employees Present:

NIEHS Staff:

Cindy Afshari, Ph.D.
Kathy Ahlmark
Beth Anderson

Lisa Archer
Martha Barnes
Linda Bass, Ph.D.
Sharon Beard
PJ Blachshear, M.D.
David Brown
Gwen Collman, Ph.D.
Allen Dearry, Ph.D.
Dwight Dolby
Dorothy Duke
Thorsten Fjellstedt, Ph.D.
Lerlita Garcia
Janet Guthrie
Jerry Heindel, Ph.D.
Zoe Huang, M.D.
Joseph Hughes
Ethel Jackson, D.D.S.
Marian Johnson-Thompson, Ph.D.
Kim Gray Kamins, Ph.D.
Elizabeth Kennington
Annette Kirshner, Ph.D.
Cindy Lawler, Ph.D.
Charle League
Edith Lee
Patrick Mastin, Ph.D.
Michael McClure, Ph.D.
Sheila Newton, Ph.D.
Liam O'Fallon
Joan Packenham, Ph.D.
Jerry Phelps
Chris Portier, Ph.D.
Marie Potoczny
Jacqueline M. Russell
Anne Sassaman, Ph.D.
Carol Shreffler, Ph.D.
Shobha Srinivasan, Ph.D.
William Suk, Ph.D., M.P.H.
Claudia Thompson, Ph.D.
Fred Tyson, Ph.D.
Bennett Van Houten, Ph.D.
Jose Velazquez, Ph.D.
Charles Wells, Ph.D.
Brenda Weis, Ph.D.
Laura Williams-Boyd
Samuel Wilson, M.D.
Michelle Winston
Carolyn Winters
Mary Wolfe, Ph.D.
Geraldine Wolfle
Jerry Yakel, Ph.D.

Other Federal Staff:

Robert Dyer - EPA
Patricia Greenwel - CSR
Rass M. Shayiq - CSR

I. CALL TO ORDER AND OPENING REMARKS

The one hundred fourth regular meeting of the National Advisory Environmental Health Sciences Council was called to order by Dr. Olden. Dr. Kelly Brix was introduced as a new ex-officio member representing the Department of Veteran's Affairs. Dr. Olden also presented certificates of appreciation to Dr. Wells, Dr. Karin (in absentia), Dr. McClain and Ms. Chuda for their participation on the council and thanked them for their service.

II. REVIEW OF CONFIDENTIALITY AND CONFLICT OF INTEREST PROCEDURES - Dr. Kenneth Olden

Dr. Olden read the requirements of the Government in the Sunshine Act. All aspects of the meeting were open to the public except those concerned with review, discussion and evaluation of grant applications and related information. The Chairperson explained policies and procedures regarding confidentiality and avoidance of conflict of interest situations.

III. CONSIDERATION OF MINUTES OF May 21, 2001, MEETING

Council accepted the minutes without change.

IV. FUTURE COUNCIL MEETING DATES

Feb 10-11, 2002 (Monday and Tuesday) in Bethesda. (to be changed to NIEHS)
May 20-22, 2002 (Monday, followed by Leadership Retreat) in Research Triangle Park.

V. REPORT OF THE DIRECTOR, NIEHS - Dr. Kenneth Olden

Dr. Olden began his report by announcing two significant personnel additions: Dr. Lutz Birnbaumer, formerly at UCLA as Scientific Director, and Dr. Chris Portier as Director, Environmental Toxicology Program. He commented on the accomplishments and qualifications of both, and expressed his thanks to Dr. Paul Nettesheim for serving as Acting Scientific Director for the past 18 months. On a more general note, Dr. Olden mentioned some key retirements and indicated concern about the large number of employees eligible for retirement and the potential impact on the Institute.

While Fiscal Year 2001 was very good, with expanded visibility for NIEHS, the Fiscal Year 2002 budget has yet to be finalized. NIH and NIEHS supporters are working for increases to continue the doubling strategy, but there are also ongoing discussions within the NIH about the implications on programs when the "leveling" begins. In addition to budget issues, other areas of Congressional interest include the Lowey/Chafee Bill to establish centers for breast cancer and the environment, whose fate is unknown at this point. Senator Clinton is interested in children's health issues, and Dr. Olden has discussed with her and her staff the NIEHS/EPA Children's Environmental Health Centers. Another of her interests is prevention, which is also a high priority for NIEHS.

Secretary Thompson has been visiting component agencies of the Department, spending up to a week on-site to get to know them. He spent a week on the Bethesda campus recently, and would like to also visit the NIEHS campus.

Dr. Olden thanked the council members who participated in the May Leadership Retreat and referred to a report contained in their folders. A staff mini-retreat to follow up on the topics presented (toxicogenomics, Parkinson's disease (PD) and women's health/fibroids) is scheduled. In addition, the Institute was a major sponsor of a conference, "Parkinson's Disease, Genes and the Environment," held in Colorado Springs in August that was very successful in bringing together different players in PD research. There have been significant advances in this area in the past 3 years, and NIEHS plans to form a consortium to move forward even more quickly.

The Institute of Medicine, with support from the NIEHS and other NIH institutes, recently released a report on gender differences entitled, "Exploring the Biological Contributions to Human Health. Does Sex Matter?" The conclusion is that sex differences are more than just hormonal, and that these differences occur on almost all levels, from the basic genetic codes to cellular mechanisms, immune system, organ functions, etc. However, these differences are not well understood and should be explored further. Dr. Olden appointed Drs. Wells and Hulka to work with the NIEHS Office of Policy Planning and Evaluation examine the report and its recommendations for opportunities for NIEHS and for coordination at the NIH level.

In Institute communication activities, Chinese language supplements to Environmental Health Perspectives have been initiated at the request of the Chinese Society of Toxicology. Certain articles will be translated and reproduced in the Chinese version. The journal has also been asked to create a second journal on children's health and the environment. The Institute has also produced updated booklets on our activities related to health disparities, Parkinson's Disease, and the intramural summer program.

Dr. Olden commented on the implications of information gained from the use of toxicogenomic and proteomic approaches, stating that they offer enormous opportunities as well as the possibility of serious misinterpretation, misuse, and abuse. He wants to insure that NIEHS is thinking ahead to deal with these questions, and is having discussions with the National Academy of Sciences to possibly set up a panel to deal with the use of information coming from the National Center for Toxicogenomics.

At a recent retreat of the Environmental Toxicology Program, the topic of the incorporation of new imaging technologies in toxicology was discussed. New novel reagents and probes are needed, as well as new indicators, labeled xenobiotics, and new reporter systems. More emphasis will be placed on this area in the coming months, working with the extramural community to advance the science and address opportunities.

In conclusion, Dr. Olden mentioned that NIEHS is actively working with the Agency for Toxic Substances and Disease Registry to identify areas of common interest. The Society of Toxicology and the nursing community are also interested in working with NIEHS. As part of our ongoing outreach activities, Town Meetings are now scheduled for Houston, Los Angeles, and Des Moines. Others are in the planning stage.

Discussion by Council members about the strategies being planned for the period after Fiscal Year 2003 when the budget doubling would end centered around concerns that NIH may not be positioned to deal with lesser increases effectively. Dr. Olden stated that questions about this issue were raised at the appropriations hearing, and he feels that we should focus on opportunities and the dollars required when dealing with questions at the congressional level, and that we also need to convince them that the dollars appropriated are being spent well.

VI. Future Directions for NIH Research in the Behavioral and Social Sciences - Dr. Kington

Dr. Olden welcomed Dr. Kington, who took over the leadership of the Office of Behavioral and Social Sciences Research (OBSSR) several months ago.

Dr. Kington reviewed the history of the Office, established in 1993 with three broad mandates: 1) enhance behavioral and social sciences research and training in the various institutes and centers, 2) expand biobehavioral research overall, and 3) improve communication. The Office has approached these mandates through the issuance of joint Request For Applications and Program Announcements in collaboration with other institutes and centers.

In 1999, the National Research Council (NRC) was asked to advise the Office on priority setting, a process that involved significant input from many communities. Dr. Kington referred Council members to the report of the NRC which was distributed to them, calling attention to the ten areas that were identified as top priorities. The remainder of his presentation focused on those ten areas and how they would be addressed. Over the next year, OBSSR will be working with NIH institutes and centers to move forward on the recommendations.

In the discussion that followed, questions were raised about review issues and how the special aspects of community-based programs were dealt with in standing study sections, how well this type of research is being integrated into the programs of the institutes and centers, how this type of research is handled by local Institutional Review Boards, and specifically, how a recent ruling by the Maryland Court of Appeals (the Kennedy Krieger lead study) might affect behavioral and social science research.

VII. Report of the Deputy Director, NIEHS - Dr. Wilson

Dr. Wilson's report focused on the real world impact of the Institute on environmental public health and mechanisms to identify opportunities and address needs of the field. As one example of mechanisms, he described the activities of an Institute of Medicine (IOM) Roundtable on Environmental Health. The objectives of the Roundtable are 1) to enhance the public's understanding of environmental health; 2) to increase opportunities for partnerships, and 3) to help the field interpret new science. The Roundtable is co-sponsored by other agencies and the American Chemistry Council, and through this mechanism, the various groups, including academic organizations, can have discussions of issues and foster collaborations while not necessarily resolving them. The work of the Roundtable includes workshops and resulting reports; regional meetings and resulting reports; special events; and briefings.

For the remainder of his presentation, Dr. Wilson reported in more detail on some of the activities of the Roundtable, including three workshops (on the definition of environmental health/links with human health, another on the environment and cancer, and a third on children's environmental health) and a regional meeting held in June of this year at the Carter Center. Activities planned for the next year are workshops on the role of environmental toxicants in premature birth, monitoring environmental health in the US, the role of the built environment in promoting human health, and a Roundtable retreat.

In subsequent discussion with the Council members, the challenges inherent in broadening the definition of "environment" were raised as were questions as to how NIEHS would respond. The Superfund Program was mentioned as an example of a broader agenda, and also as nutrition, behavior, and communication and consensus-building activities. One member also pointed out that review committees need also to have a broader view of environmental health, and that this should be considered in assignment of applications to NIEHS as well.

VIII. The First National Allergen Survey: Preliminary Results - Dr. Zeldin

Dr. Zeldin began his presentation by reminding the Council that asthma is a public health issue of increasing importance, increasing incidence, and increasing visibility. It is also a good example of a disease with a significant gene-environment interaction that is amenable to study. He has been leading a project in the Division of Intramural Research in collaboration with ongoing work of the Department of Housing and Urban Development's lead survey to collect samples for analysis of various allergens and their association with asthma incidence. This project is described in the abstract at attachment B.

The Council expressed interest in and support for this project and had a number of questions for Dr. Zeldin about his findings.

IX. Nictoinic Receptors in the Rat Brain: Role in Neuronal Signaling and Alzheimer's Disease - Dr. Yakel

Dr. Yakel began by describing in general the importance of cell receptors in nerve cells, particular in the brain, focusing on the neurotransmitter receptor, synaptic signaling and communication, and diseases caused by dysfunction in these receptors. He noted that nicotine is one of the most prevalent and potent neurotoxins, but it has some positive functions as well. Therefore, studying its action and receptors has potential for the development of new therapeutics. His laboratory focuses on the structure of the receptor, its molecular and functional characteristics, and its regulation. An abstract of his presentation is found at attachment C.

X. Environmental Genome Project Update - Dr. Velazquez

Dr. Jose Velazquez, Chemical Exposures and Molecular Biology Branch, provided Council with some background on this Institute-wide initiative, focusing on the status of the extramural component and in particular, a database called dbSNPs, for Single Nucleotide Polymorphisms. NIEHS plans to increase the rate of resequencing environmentally-responsive genes from

20/year on 450 individuals to 70 genes/year with an infusion of additional funds. Current estimates are that the project will eventually resequence 300 genes at the 450-person level.

Council members expressed strong support for this initiative, and inquired as to how NIEHS will prioritize integration of information resulting from the toxicogenomics initiative. Dr. Velazquez responded that we expect to focus on pathways. Other discussions points were whether limitations were primarily available capacity or dollars; quality of the data; and the potential value of an oversight body to help make decisions regarding a number of issues inherent in this sort of program. Staff agreed to take this latter recommendation under advisement.

XI. Review of Superfund Program - Dr. Thompson

Dr. Thompson stated that this was the first of several presentations to familiarize Council with the Superfund Basic Research Program, and she introduced other staff involved with the Program. She reported on some of the implications of the direct appropriation, as opposed to previous years of the Program's history when funds went through the U.S. Environmental Protection Agency (EPA), and the opportunities this presents for program stability and, hopefully, growth. The President's Budget for Fiscal Year 2002 gives the Program an 11% overall increase, and a new aspect will be the addition of SBIR initiatives in both the research and worker education and training components.

Dr. Thompson's presentation focused on products and specific outcomes of the program, especially on technology. She gave several examples of technologies developed within the Program and the impact these have had on EPA and the clean-up process.

In the discussion that followed, the Institute was commended on the inclusion of local outreach in the Program, its responsiveness to the political process, and the management of a model of multidisciplinary research.

XII. Validation of the Toxicogenomic Approach-Dr. Afshari

Dr. Afshari described some of the new challenges and opportunities facing toxicology, including how to get new technologies into the field and the National Toxicology Program (NTP) and how to improve efficiency. Toxicogenomics represents the union between toxicology and genomics and as such is a very powerful tool allowing global analysis of the genome. The potential impact of the technology lies in the ability to increase our understanding of the effects of mixtures, of low dose exposures, chronic vs. acute exposures, effect of genotype, the interplay of nutrition and other factors on exposures, and many other such factors. Approaches include RNA expression, linked with bioinformatics, and later with proteomics and pathology profiles. The NTP and NIEHS are in a unique position to meld information from new technologies with a wealth of toxicology and pathology data from the NTP.

Dr. Afshari summarized for the Council various techniques and technologies used in the NIEHS Microarray Center, which she heads. The Center currently uses "chips" containing the entire yeast genome, 12,000 human genes, and genes from the mouse, rat, and xenopus. Information from the use of these chips may be useful in hazard identification among thousands of

compounds, especially when used in conjunction with histopathology and other endpoints through informatics, and this will be valuable information in a publicly available database. The abstract of Dr. Afshari's presentation is at attachment D.

The Microarray Center set out to validate the toxicogenomic approach, asking the question of whether gene expression profiling can classify unknown agents. Preliminary results look quite promising, in that 22/23 unknowns were correctly classified. With the approach validated, the Center will now focus on the identification of profiles associated with different toxicities or disease expression as well as new studies related to mechanisms. Hopefully, all this will lead to the development of a "virtual toxchip" with genes from various pathways and various effects. The Center also hopes to develop high through-put, cost effective screens.

XIII. Report of the Director, DIR and Report of Board of Scientific Counselors - Dr. Nettesheim and Dr. Marnett - Closed Executive Session

This portion of the meeting was closed to the public for the presentation of the Report of the Board's review of the Laboratory of Molecular Genetics and the biostatistics and epidemiology branches in the Divison of Intramural Research. A copy of the written Report of the Director, Division of Intramural Research, can be found as attachment E.

XIV. Report of the Director, DERT - Dr. Sassaman

Dr. Sassaman introduced new extramural program staff attending Council for the first time, and also called attention to items in the Report of the Director, DERT at attachment F, especially the "significant papers," which represent the "products" of the extramural research portfolio. She then gave a brief presentation on the potential impacts of far smaller budget increases anticipated with the end of the 5-year budget doubling period after Fiscal Year 2003. The NIH has begun discussions on steps that can be taken to assure stability in this post-doubling period, or a so-called "soft landing." After summarizing some of the modeling done by NIH and the related assumptions, she reviewed some options that could be taken by NIEHS at the institute level. She ended this part of the presentation by suggesting topics that the Council might consider further, including whether the success rate of the Research Project Grant budget line represents an adequate measure of the Institute's ability to meet its objectives, and whether current mechanism distributions represent the best allocation of funds to support new opportunities and needs for environmental health sciences.

In concluding the Director's Report, Dr. Sassaman advised the Council that the Worker Education and Training Program has begun a strategic planning process that began with a meeting of "champions" on September 5 and includes meetings to get input from other stakeholders in the Program, including the principal investigators and other Federal Partners.

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).

There was a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions, or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect.

XV. REVIEW OF APPLICATIONS

The Council considered 260 applications requesting $78,914,229 in total cost. The Council recommended all 260 applications with the total cost of $78,914, 229.

XVI. ADJOURNMENT OF THE NAEHS COUNCIL

The meeting was adjourned at 10:30 a.m. on September 11, 2001.

ATTACHMENTS

A. Council Roster
B. Abstract - Dr. Zeldin In *Adobe Acrobat* Format
C. Abstract - Dr. Yakel In *Adobe Acrobat* Format
D. Abstract - Dr. Afshari In *Adobe Acrobat* Format
E. Report of the Director, DIR In *Adobe Acrobat* Format
F. Report of the Director, DERT In *Adobe Acrobat* Format