Department Of Health And Human Services
National Institutes Of Health
National Institute Of Environmental Health Sciences

Minutes of The National Advisory Environmental Health Sciences Council
February 14-15, 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 meeting was open to the public on February 14, 2005, from 8:30 a.m. to 5:30 p.m. and on February 15, 2005, from 8:30 a.m. to 9:50 a.m. in accordance with the provisions of Public Law 92-463. The meeting was closed to the public on February 15, from 9:50 a.m. to 11:40 a.m. for consideration of grant applications. Notice of the meeting was published in the Federal Register.

Members Present:

Douglas Benevento, J.D
Deborah Brooks
Teresa Bowers, Ph.D.
Charli Coon, J.D.
Joan Cranmer, Ph.D.
Elaine Faustman, Ph.D.
George Friedman-Jimenez, M.D
Michael Gallo, Ph.D.
Frederick P. Guengerich, Ph.D.
David Losee, J.D.
Martin Philbert, Ph.D.
Peter Spencer, Ph.D.
Frank Talamantes, Ph.D.
Peter Thorne, Ph.D.
James G. Townsel, Ph.D.

Members Absent

Dale Eastman
Bernard Goldstein, M.D., Ph.D.
George Gray, Ph.D.

Ex Officio Members Present

COL James S. Neville

Liaison Members Present

Olivia Harris - Alternate. (National Center for Environmental Health, ATSDR, CDC)
Marion Ehrich, Ph.D., (Society of Toxicology)
David Ringer, Ph.D. (American Cancer Society)

Liaison Members Absent:

Drue Barrett, Ph.D., National Center for Environmental Health, ATSDR, CDC)
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
David Balshaw, Ph.D.
Martha Barnes
Linda Bass, Ph.D.
Lutz Birnbaumer, Ph.D.
David Brown
Gwen Collman, Ph.D.
Allen Dearry, Ph.D.
Dorothy Duke
Sally Eckert-Tilotta, Ph.D.
Richard Freed
Jerrold Heindel, Ph.D.
Michael Humble, Ph.D.
Ethel Jackson, D.D.S.
Laurie Johnson
Marion Johnson-Thompson, Ph.D.
Annette Kirshner, Ph.D.
Dennis Lang, Ph.D.
Cindy Lawler, Ph.D.
Charle League
Carolyn Mason
Patrick Mastin, Ph.D.
Rose Anne McGee
Teresa Nesbitt, DVM, Ph.D.
Ted Outwater
Christopher Portier, Ph.D.
Leslie Reinlib, Ph.D.
James Remington
Margarita Roque
Anne P. Sassaman, Ph.D.
Carol Shreffler, Ph.D.
William Suk, Ph.D., M.P.H.

Claudia Thompson, Ph.D.
Bennett Van Houten, Ph.D.
Charles Wells, Ph.D.
Brenda Weis, Ph.D.
Leroy Worth, Ph.D.

Other Federal Staff:

Ghenima Dirami, Ph.D., CSR/NIH
Patricia Grenwel, Ph.D., CSR/NIH
Timothy Hays, Ph.D., OER/NIH
Sheila Johnson, NIMH/NIH
Michael Martin, Ph.D., CSR/NIH
Christine Melchior, Ph.D., CSR/NIH
Laura K. Moen, Ph.D., NIGMS/NIH
Elliot Postow, Ph.D., CSR/NIH
Joseph Rudolph, Ph.D., CSR/NIH
Norkia Ruiz-Bravo, Ph.D., OD/NIH
Brent Stanfield, Ph.D., CSR/NIH

Members of Public Present

Marilyn Massey-Ball, Masimax Resources, Inc.
Bobbie Peterson, Computer Sciences Corporation

Guest Speakers

Dr. Deborah Nickerson, Department of Genome Sciences
University of Washington
Seattle, Washington

Dr. Kenneth Ramos, Department of Biology and Molecular Biology
University of Louisville
Louisville, Kentucky

Dr. Roger G. Ulrich, Senior Director
Rosetta Inpharmatics, LLC (Merck & Co., Inc.)
Seattle, Washington

I. CALL TO ORDER AND OPENING REMARKS

Dr. Kenneth Olden called the one hundred twelfth regular meeting of the National Advisory Environmental Health Sciences Council to order. He noted those members of Council who were not present and added that the slate of new members had been approved. He then presented Certificates of Appreciation to the retiring Council members (Drs. Cranmer, Friedman-Jimenez, Gallo, and Guengerich). Ms. Eastman, not present, will receive her certificate by mail. Dr. Olden

acknowledged the presence of Dr. David Schwartz, an observer at this meeting, who will take the position of Director of NIEHS on April 4, 2005. Members of Council introduced themselves. Dr. Anne Sassaman introduced Mr. Brian Moyer who is with the Division of Extramural Activities Support (DEAS); she also brought to the attention of Council the need to sign their Conflict of Interest form and to complete their travel vouchers expeditiously.

II. REVIEW OF CONFIDENTIALITY AND CONFLICT OF INTEREST PROCEDURES

Dr. Olden discussed with Council the method of voting 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 September 13-14, 2004, meeting were approved as amended; Dr. Elaine Faustman was not present at the September meeting.

FUTURE COUNCIL MEETING DATES

The following dates for May and September were confirmed

May 26-27, 2005 NIEHS Thursday Friday (No Leadership retreat)
September 1516, 2005 NIEHS Thursday Friday
February 2006 meeting dates are to be determined

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

Dr. Olden began by sharing Dr. Schwartz's biographical sketch and spoke of his many outstanding attributes.

He then presented the budget report. Congress approved a 3% increase in the budget. He provided comments on the budget taps by the Department of Health and Human Services (DHHS) and the National Institutes of Health (NIH). He also reported that the Research Project Grants (RPGs) are holding steady, non-competing will be funded at the committed level, and the average cost of an RPG is approximately $330,000. NIEHS is contributing 4.1 million dollars to the Roadmap initiative.

The President's budget for Fiscal Year 2006 emphasizes four areas of interest: 1) biodefense, 2) HIV/AIDS, 3) Roadmap initiative, and 4) neuroscience.

The Senate hearings are scheduled for early April; however, the House hearings have not yet been scheduled. Their hearings will possibly take place in April or later due to the reorganization of the appropriation subcommittees. The Veterans Administration, Housing and Urban Development, and Other Agencies subcommittee has been eliminated; therefore, the Energy and the Environment subcommittee will hold budget hearings for Superfund appropriations.

Dr. Olden mentioned two major issues being discussed at NIH. The first, the NIH Public Access Policy, is scheduled as a presentation today, and the second, the Conflict of Interest Policy.

In his report on the Conflict of Interest policy, he hoped to clarify allowable (or permitted) activities. It was thought that scholarly activities, collaboration, and teaching were not permitted. All of these activities are permissible, but must be performed as government-related activities. Therefore, compensation cannot be received for these activities. This is an interim policy and comments are being solicited through the Federal Register. NIH will review this policy, and its impact on the retention and recruitment of the best scientists. Next year NIH and the Secretary of DHHS will look at these interim guidelines and make changes where necessary.

The next topic reported on was Data Quality Management issues. NIH received eight Data Quality Management requests. Six of these have been for the National Toxicology Program (NTP). Agencies that have responsibility for making recommendations about policy and produce documents that take position on issues receive these inquiries. Three agencies within the DHHS (Food and Drug Administration (FDA), Centers for Disease Control (CDC), and NIH) do this. An example, the Report on Carcinogens (ROC) that is produced every two years by the NTP, lists the number of substances that have been peer-reviewed and published with the Secretary of DHHS's endorsement. Enquiries on data quality require a huge investment of time and human resources.

The NIH Roadmap was mentioned and consists of three themes: New Pathways to Discovery, Research Teams of the Future, and Re-engineering the Clinical Research Enterprise. A handout had been given to Council. Consistent with the Research Teams approach, Congressional language mandated that the National Science Foundation (NSF) and NIH develop interdisciplinary research and scientist teams to identify the broader problems. Two conferences (NIH and NSF) were held this year. The National Academy of Science released a report supporting the interdisciplinary team approach. Restructuring of study sections is also consistent with this theme. The question of how to maintain a balance between single research projects and interdisciplinary research still remains.

Three recent NIEHS publications were brought to the attention of Council. Dr. Olden directed Council to the NIEHS Home Page "Recent Advances." He encouraged Council to follow the research contributions of NIEHS via this medium. He also directed Council to the handout they received. Dr. Olden mentioned three studies of interest. The first study, published in Science, "Shoe Factory Workers in China" was conducted by Martyn Smith, et. al. The study noted that the glue used in the manufacturing of shoes contains benzene and that the low levels of benzene caused some toxicity in the blood cells. The white blood cells, platelets, and colony forming potential of bone marrow cells were significantly decreased. The significance of the study is that occupational exposure is regulated at 1ppm and the study found toxicity at levels lower than 1ppm. Therefore, further studies will be conducted and regulatory agencies will look at the data to determine if there will be a need for more rigorous occupational standards.

The next study presented to Council, "herbal supplements" published in Toxicological Sciences, was conducted by Dr. Abraham Nyska, (NIEHS/NTP). He discovered that a combination of ephedrine and caffeine causes damage to the heart muscles (hemorrhaging and necrosis) and

death in the rat. This finding may be a possible explanation for sudden deaths in humans that have had this combination of herbal supplement.

Dr. Daniel Baden, University of North Carolina at Wilmington, conducted the final study presented to Council. In this study, he found an anti-toxin in the red tide algae, which shows promise in the treatment of cystic fibrosis. This study generated considerable press.

Complements were bestowed on Christine Bruske (Communications Director) who has been at the Institute for six months. Her effort on the media campaign for the Sister Study has been outstanding. The visibility and image of the Institute, under her direction, will dramatically change in a positive way.

Dr. Olden reported on two new NIEHS contracts. The first contract was awarded to Perlagen Sciences to sequence fifteen most commonly used mouse strains. The purpose of the contract is to find out what negative mouse strains are relevant to developing cancer in humans. The goal of the second contract is to develop an RNAi library, which will be a resource library of RNAi knockout genes. The importance of the library is to be able to inactivate the specific gene responsible for an environmentally related disease. This information will be made available to the public.

Dr. Olden concluded his report by informing Council that The Scientist magazine conducted a survey on the best places to do postdoctoral research in the United States. NIEHS in 2004 was rated number three and in 2005 was rated number four, concluding that NIEHS has given its postdoctoral students a positive experience.

Council-Initiated Discussion: Discussion centered on such issues as the projection of an increase in the RPG success rate in FY06, and the Congressional mandate for NSF and NIH to develop interdisciplinary research and scientist teams. In response to the discussion, Dr. Olden attributed the RPG success rate to the excellent management skills of the Division of Extramural Research and Training (DERT) and the congressional mandate was part of the appropriations language.

V. NIH Public Access Policy Dr. Norka RuizBravo

Dr. Sassaman introduced and welcomed Dr. RuizBravo to the Council. Dr. Ruiz-Bravo presented the new NIH Public Access Policy. The policy enhances public access to archived publications resulting from NIH-funded research. Beginning May 2, 2005, NIH-funded investigators are requested to submit to the NIH National Library of Medicine's PubMed Central an electronic version of the author's final manuscript.

This policy applies to all research grant and career development award mechanisms, cooperative agreement, contracts, Institutional and Individual Ruth L. Kirschstein National Research Service Awards, as well as NIH intramural research studies.

The policy hopes to: 1) ensure the permanent preservation of published research findings, 2) provide a better searchable compendium for NIH and its awardees, and 3) make the published

results more readily accessible to the public, health care providers, educators, and scientists. It will also enable staff to better understand their research portfolios, monitor scientific productivity, and help to set research priorities.

Council-Initiated Discussion: Dr. Ruiz-Bravo's presentation generated a number of questions. Concerns primarily centered around issues related to tracking, RPG success rate, copyright laws (U.S. and foreign), training on the copyright laws, stage of manuscript submittal, financial and the monetary impact the new policy would have on investigators and journals. The discussion concluded with the understanding that before any of these questions can be answered the policy needed to be further evaluated.

VI. Environmental Genome Project Overview Dr. Deborah Nickerson

Dr. Olden introduced and welcomed Dr. Nickerson who is a principal investigator at one of the five components of the Environmental Genome Project (EGP). She began her presentation by stating that the next challenge will be to understand the link between DNA sequence (genotype), biology (phenotype), and the environment. Susceptibility to common diseases is thought to arise from these multiple factors, each conferring a low relative risk for disease. She added that since the risk of any given effect is small, detecting these disease risks would require large samples, making population-based association studies more practical for tracing the underlying susceptibilities. Therefore, the EGP was developed to scan environmental response genes involved in DNA repair, cell cycle control, apoptosis, drug metabolism, and other pathways in order to explore the relationship between environmental exposure and genetic susceptibility in the etiology of common disease.

Dr. Nickerson then presented an update of the EGP which included: illustrations of how high-density maps provide valuable resources for association mapping of genotype-phenotype-environment interactions; the identification of potentially functional polymorphisms in environmental response genes; and the development of new tools, views, and strategies to improve the discovery of genetic variations associated with sensitivity to environmental agents.

Council-Initiated Discussion: Discussion centered on the need for comparative approaches to define or identify areas of stability across the genome; whether the focus should be on promoter or splice segments; and the need for both interdisciplinary teams and databases to access the volume of information being generated. In response, Dr. Nickerson stated that we are now looking at noncoding regions across all species. This has been problematic, so we now need to focus more on interspecies variation. She also suggested that we should be looking at conserved regions of the genome and not just the promoter or splice segments. She further stated that the formation of interdisciplinary teams will require additional training, and that type of training is still being developed. Finally, she acknowledged the need to develop databases that are easy to access and useful to the clinicians and investigators who would benefit and utilize the information provided.

VII. NIH Roadmap Overview Dr. Dushanka Kleinman

Dr. Olden introduced Dr. Kleinman as the individual most informed on the Roadmap initiative. Dr. Kleinman thanked Dr. Olden for his role as co-chair of one of the nine Interdisciplinary Research Working Groups overseeing the implementation of the Roadmap. She also introduced Dr. Allen Dearry as the Institute liaison for the Roadmap initiative.

Dr. Kleinman gave an Overview of the NIH Roadmap Initiative. She spoke about the history and purpose, steps in the process, and the major NIH Roadmap themes.

She stated that Dr. Zerhouni's vision is to chart a "roadmap" for medical research in the 21st century. The purpose is to identify major opportunities and gaps in biomedical research that no single institute could tackle alone, but the NIH as a whole could. The objective is to make the biggest impact on the progress of medical research.

Steps included meetings with NIH directors, Working Groups, and Implementation Groups. These groups looked at the challenges, they set the priorities, and discussed how the roadmap would be implemented.

The major Roadmap themes are: 1) New Pathways to Discovery (the need to advance our understanding of the complexity of biological systems), 2) Research Teams of the Future (the complexity of biomedical research problems of today demand that scientist explore new organization models for team science), and 3) Re-engineering the Clinical Research Enterprise (there is a need to develop new partnerships of research with organized patient communities, community-based health care providers, and academic researchers). The ultimate goal of the Roadmap initiative is to more fully involve and empower the public in the research process.

Council-Initiated Discussion: After Dr. Kleinman's presentation the discussion focused on the lack of specific preventive, diagnostic and therapeutic interventions in the Roadmap initiative and the role of NIEHS in the reengineering of the clinical research initiatives. In response to the interventions, she stated the Roadmap was not designed to look at specific interventions, but at the underpinnings of the research that would lead to the specific interventions. In reference to the reengineering issues, she stated that they are generic to every institute and therefore, germane to the NIEHS.

VIII. Future Vision for National Toxicology Program (NTP) Dr. Christopher Portier

Dr. Olden introduced Dr. Portier, the Associate Director of the NTP. Dr. Portier began his presentation by informing Council that the work done by NTP complements the work of NIH, EPA, and FDA. He described the background, membership, and functions of the NTP. The functions are: 1) nominations, 2) toxicology research operations, 3) evaluation, 4) scientific oversight, and 5) review and outreach. These functions help us to understand the NTP Roadmap. He then proceeded to summarize recent activities of the NTP, such as the release of a publication on ephedrine and caffeine in the 11th Report of Carcinogens, NTP chronic exposure studies as they relate to cardio-evaluation and neurotoxicity, genomic issues, and the C. elegans project.

He presented the vision for the NTP. The NTP hopes to move toxicology from a disease-specific animal testing program into a more mechanistic-based approach program that looks at specific

aspects of the mechanism that leads to the disease. The objective will be to find a commonality in those mechanisms and challenge those mechanisms with environmental agents to try to turn toxicology into a more predictive science. This would allow a broader spectrum of compounds to be tested for the same amount of money with a higher public health impact and safety.

In August 2004, NTP held a retreat to look at the Roadmap draft for the NTP. The participants were from government agencies, the academic community, industry stakeholder groups, and public groups that were interested in the activities of the NTP. Four broad areas emerged from the retreat: HighThroughput Screening, Bioassay Review and Redesign, MediumThroughput Screening including Toxicogenomics and Proteomics, and Data Analysis and Interpretation. This group developed a final draft of the Roadmap document and developed an "activity matrix" of key activities and priorities for the next five to ten years.

Dr. Portier concluded by showing the very dynamic change that has occurred to the NTP. He pointed out that the NTP participates and works well with multiple agencies at all levels for one common mission to improve the scientific base for regulatory decisions in public health. NTP is going to a multitiered testing program (high-throughput screening, mediumthroughput screening, multigenerational chronic exposure studies, etc.) using mammalian systems. This is a good science-based approach to toxicology that leads to a more efficient utilization of resources.

Dr. Olden then asked Dr. Portier to explain the Congressional mandate for NTP. Dr. Portier stated the mandate had two parts, the first part deals with toxicology testing for the US government in areas where there are no legal mandates for testing. The second part is to advance the science of toxicology (cutting-edge science in support of public health decisions). (NTP Report available upon request)

Council-Initiated Discussion: The discussion centered on new areas being reported in the ROC. These areas included human viruses (hepatitis B, C, and the papillomavirus), alcohol and alcoholic beverages, and radiation. Comments were made about the criteria to answer the mechanistic questions and communication to the public on risks.

Questions centered on how validation would be done and how predictability will improve. What is the status of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)? How will NTP improve the predictability of pathophysiology/diseases associated with toxins, has this been piloted, and are there data?

To answer the question on validation, Dr. Portier stated there were different levels of validation. The various methods of validation will need to be discussed at workshops to look at the aspects of prediction and whether we can validate or not. On the status of alternative methods for animal studies, ICCVAM's progress has been slow. However, since ICCVAM's inception five to six assays have been validated. In reference to the predictability of diseases associated with toxins, this has not been looked at by NTP; however, the International Life Sciences Institute has done a few toxins.

IX. Toxicogenomics Dr. Roger Ulrich

Dr. Olden introduced Dr. Ulrich as a scientist from industry (Rosetta Inpharmatics LLC) whose mission is to discover and develop safer drugs with less toxicity. In pursuing this mission Dr. Ulrich has developed an appreciation for toxicogenomics.

Dr. Urlich informed Council that toxicity remains a major reason to pipeline attrition and termination of development programs for new pharmaceuticals, accounting for nearly a third of all drug candidate failures. Reducing or ameliorating toxic liabilities, preferably early in the discovery phase, can increase the probability of success for new drug candidates and ultimately improve product safety. He noted, to achieve this effectively requires knowledge of toxic mechanisms and off-target effects for each new drug candidate and its metabolites (and species differences where they exist), identification of discriminating and predictive biomarkers, and an understanding of both phenotypic diversity and individual risk factors within the human population. He pointed out, while still in the formative stage, toxicogenomics is already helping to meet these requirements. Currently, large-scale monitoring of gene expression is effectively being done using microarrays which, along with informatics provides for the transcriptional evaluation of thousands of genes at one time. Analysis of gene expression profiles obtained from target tissues following drug or chemical exposure reveals several distinct characteristics for each compound; a transcript signature can define each characteristic. Using a compendium of expression profiles, compound-specific effects for new chemicals can be compared to responses for known and characterized compounds to help identify toxic liabilities even when gene annotations are incomplete or inconclusive. Further, examination of discrete gene responses where annotations exist can provide specific mechanistic insights through the identification of response pathways. Discrete gene changes can also help identify putative biomarkers, and in preclinical toxicology, the expression profile itself may serve as a diagnostic or prognostic biomarker. Dr. Ulrich concluded his presentation by saying, toxicogenomics has enable the toxicologist to more effectively identify compound hazards and mechanisms, and may eventually help better predict human risks.

Council-Initiated Discussion: The discussion focused on the following points and their associated responses:

1) When do you think the crossover point, (dollar wise and time wise) will come from information gathered using multiple animal species to predict human outcomes to using microarray toxicogenomics, proteomics and metabolomics?

From a dollar standpoint the tools are available and there has been a ten-fold drop in cost. Over the next year this trend will continue. In terms of a timeline, it will take at least three to five years to get sufficient peer-reviewed basic science data that can ultimately be transferred to mainstream research.

2) Is the methodology geared to predict the risk factors for individuals at risk?

At this time, the process is slow; one needs to understand the risk factors associated with a drug in the general population. We are doing one gene at a time, one pathway at a time, as the search for applicable biomarkers is both time-and labor-intensive. However, with the advent of such biomarkers (signatures), there will be a paradigm shift as this is applied to target populations, in

terms of genetic traits and confidentiality. Without a doubt, there will be the need to use one's phenotype as a means to identify risk factors.

3) To what extent might we advance our understanding of mechanism of toxicity by a combination of proteomic and genomic studies?

Currently there is no single approach to examine the issue of environmental insult(s). Nonetheless, transcriptomics in toxicogenomics works. All the same, more work needs to be done with proteins, because a transcriptional response alone does not give enough information. Therefore, given that studies associated with the proteome have narrowed, there are still notable limitations in practical day-to-day analysis methods. Nonetheless, it is an area that is still awaiting the technological break through to make it a routine laboratory procedure.

X. Impact of Center for Scientific Review (CSR) Study Section Realignment on NIEHS Applications Drs. Brent Stanfield and Michael Martin

Dr. Sassaman introduced Dr. Brent Stanfield, acting Director of CSR and Dr. Michael Martin, a Division Director within CSR. She noted that Dr. Martin has been working very closely with the NIEHS' extramural community to address concerns regarding the referral of applications.

Dr. Stanfield began his presentation by informing Council that CSR is one of 27 Institutes and Centers at NIH. CSR is entirely a service Center where all applications are sent for receipt and referral, whether they will be reviewed by CSR or the Institute. He gave a brief history of the genesis of the Panel of Scientific Boundaries for Review Reorganization (PSBR). The panel was charged in April 1998 with recommending how peer review should be organized in order to review research appropriately at that time, and to be able to anticipate future changes. Their report in January 2000 stated that the review process to be outstanding, needed to set high standards, contribute to the advancement of the health-related science, encourage innovation and risk taking, exercise fairness, be transparent to all participants, and undergo periodic review. To accomplish these goals it was recommended that a new organizational structure of Integrated Review groups (IRGs) be developed that would focus on broader perspectives, rather than spot-on expertise. An additional goal was to move basic science towards specific organs/diseases when possible, create several cross cutting clusters, as well as maintain a set of study sections to handle basic science and applications concerned with multiple organs/diseases.

Dr. Stanfield reported on the progress to date. Guidelines for 98 study sections in 16 IRGs were developed. To date 14 of the 16 reorganized IRGs (86 study sections have already had their meetings). The final phase of the reorganization will be completed February/March 2005. The final two IRGs are: Biological Chemistry and Macromolecular Biophysics (BCMB) and Cell Biology (CB). Twelve new study sections are within these IRGs.

Dr. Stanfield concluded that CSR would continue to review the functioning of the new IRGs and study sections on a five-year cycle. These assessments will be planned with input from the scientific community, NIH program and review staff, and by an outside working group. This working group will send its report to a newly constituted committee, the Peer Review Advisory Committee, for review and evaluation.

Dr. Martin informed Council that his presentation would try to address some of the concerns expressed by the communities they represent. CSR took two Council rounds, May 2000 and October 2002. Using all R01 applications, the applications were tracked by where they were reviewed, and where they would be reviewed if the PSRB guidelines were followed. These applications were the control group and the ES R01's were the comparison group. After all the data were examined, the outcomes for toxicology applications (former ALTX ES R01s) before and after the reorganization are relatively constant.

Council-Initiated Discussion: A number of questions were asked about the data and reorganization. It was concluded that the data as presented showed little difference in the review of ES R01 applications. The reorganization has spread the ES applications across a large number of study sections, and it is difficult for program staff to be at the reviews, thereby impacting on their ability to develop continuity with the study sections and to hear the reviews first hand. However, it was mentioned that clustering was not the answer because that imposed other review problems. It was noted that the toxicology community has been very vocal about the reorganization and their comments are being evaluated and acted upon, where possible. In conclusion, Council was advised to relay other issues or ideas for CSR's review to Dr. Sassaman who will forward them to CSR.

XI. Report of the Director, DERT Dr. Anne P. Sassaman

Dr. Sassaman informed Council about the Division of Extramural Activities Support (DEAS) and the new travel agency (Omega) and their impact on DERT and Council operations. She directed the attention of Council to the section of the Agenda Book that contained the "Featured Activities of DERT," which informs the Council on what DERT staff is doing and the highlighted research and science of the extramural community. She encouraged Council to take a moment to look at this section. She mentioned that in March, Sue Haithcock, who had been a long time employee of DERT (15 years), would be retiring. Michelle Qwens was thanked for the excellent job she did in preparing for Council even with the stresses and demands of a family crisis. She also congratulated Dr. James Townsel on his coming induction as a Fellow of the American Academy for the Advancement of Science (AAAS).

Dr. Sassaman presented the Award and Budget report for FY04. NIEHS appropriations for FY04 and FY05 have remained flat and the budget numbers are approximately the same. The report showed what NIEHS was able to accomplish with the allocated budget. She spoke about the FY04 expenditures, the bulk of the expenditures are in grants (50%); the remainder Intramural (26%), Contracts (21%) and RM&S (3%). She showed how the FY04 extramural grants expenditures were distributed; RPGs (71%), Centers (14%), Training (6%), other research (6%), and SBIRs (3%). It was also noted that the Superfund dollars are through a separate appropriation and this mechanism is a large component of the extramural activities (20%). She pointed out that the FY04 RPG total budget was $213,351.

Dr. Sassaman discussed the RPG success rate beginning with FY97. In FY97 the RPG success rate was 18% compared to NIH, which was 30%, this trend continued until FY 02 when NIEHS began to closely approach the NIH success rate. However, in FY04, with the flattening of the budget and the obligated commitments due to the doubling of the budget, NIEHS funded only a

129 grants. This is five more grants than FY03, which accounts for a slight drop in RPG success rate in FY04 given an increase in the number of applications. It was pointed out that the RPG line presented represents a combination of those applications submitted in response to RFAs as well as investigator-initiated grants, and there was essentially no difference in the RPG success rate for either one.

The next topic presented to Council was the Biennial Advisory Council Report (this was sent in advance to Council for their review). This document is informational to Council and is also to certify compliance with NIH policy of inclusion of women and minorities in research. The legislation mandates that the Advisory Council of each Institute certify compliance with this policy every two years. The extramural staff has a responsibility that no award is made for an application with human subjects until all the requirements for tracking and the inclusion have been met. Once Council certifies the Biennial Report, the Institute Director must certify that Council has reviewed it. A motion was made for approval, seconded and unanimously approved.

Dr. Sassaman brought to the attention of Council the document, Council Delegated Authorities and Guidelines for Staff Actions, which was included in the meeting materials. NIH policy requires an annual review by Advisory Councils of the delegated authorities and operational guidelines under which institute staff operate. These guidelines fall into two general categories. First, Council-delegated staff actions are actions delegated to staff that require no follow-up action with Council. Second, Council delegates to staff certain operational actions that are required to ensure the smooth operations of the extramural division in conducting business with NIEHS grantees; these actions require the establishment of a threshold level for Council involvement. A motion was made to accept the Council Delegated Authorities and Guidelines for Staff Actions as modified for another year. The motion was seconded and unanimously approved.

Dr. Sassaman then introduced Dr. Leslie Reinlib, a Program Administrator in the Susceptibility and Population Health Branch. Dr. Reinlib presented an update on the Breast Cancer and Environment Research Centers. He informed Council that the four Centers were created in September 2003. Their primary goal, while using the latest technology, is to provide a better understanding on how environmental influences can alter the future risk of breast cancer. The Centers are comprised of two major scientific projects in the areas of biology and epidemiology. The biology projects will look at promising toxins or chemicals that might alter either the age of onset or the progression through puberty, as well as using laboratory animal models to study tumors in depth. The epidemiology projects are being carried out on 1200 girls across the United States and will examine how different environmental factors and foods can alter either the onset or the progression through puberty. Each Center also has a Community Outreach and Translation Core, which is a liaison between the Center, local communities and breast cancer advocates. The Centers are being guided by a subcommittee of Council, the Breast Cancer and Environment Working Group, which includes Dr. Gallo, Ms. Eastman, and representatives from the National Cancer Advisory Board, a partner in this endeavor. A folder containing additional information was given to Council.

Dr. Gallo, a member of the working group, gave a brief history of the program. The underlying hypothesis of the Centers is that early life events in women can determine, at least in part,

susceptibility for breast cancer. He pointed out that across the consortium interdisciplinary researchers are focusing on a common theme, the environment and breast cancer and that some of the early research problems have been addressed. A standardized approach has been developed across the Centers, which becomes an important issue when the data are being analyzed. He concluded that the Community Outreach groups have done an excellent job in promoting the Centers and the Centers are making great progress.

Council-Initiated Discussion: Questions and comments centered on the comments made by Dr. Gallo. How do you get the participants of the Centers to develop a standardized approach? Are there concerns that the progress in recruiting children for the epidemiology studies has been difficult and slow?

It was pointed out to Council that these Centers are funded under a cooperative agreement and they can be guided by staff. The recruiting of children into studies is always a slow process and may take more time then originally envisioned.

XII. Assessment of NIEHS P30Centers Program Dr. Martin Philbert and Dr. Kenneth Ramos

Dr. Sassaman gave a brief introduction and background of the P30 Core Centers. Drs. Martin Philbert and Kenneth Ramos presented a summary of the report from the Assessment Working Group of the P30 Centers. This was the first evaluation of a program that has existed for many years. They discussed the impact and national visibility of the program, the pros and cons of incremental funding, and the lack of flexibility within the program (expansion, contraction, assignment of resources). In addition, they noted the successes of the program and opportunities for improvement.

The recommendations made by the Assessment Working Group were as follows: Improve impact and national visibility through documentation and dissemination of accomplishments, and translation of basic research into clinical and/or behavioral outcomes. In future evaluations there need to be periodic reviews looking at the type, breadth, and depth of the Centers in the NIEHS portfolio, input from stakeholders, and creation of databases that allow for easy retrieval of information. Incremental increases in funding are needed to increase budgets to match increased expectations, to give flexibility in building the environmental health research portfolio, and to enhance the outreach and pilot project programs. The working group members recommended considering the creation of Comprehensive Centers that complement the existing Core Center Program, and the promotion of Regional Centers.

Improvement in the Center's program can be envisioned in the areas of better documentation of accomplishments, further discussion of the impact of the science, and enhanced identity of the Centers. (Centers report available upon request)

Council-Initiated Discussion: Comments focused on the tension between science of the more applied Centers and high visibility areas, as well as interactions with local constituents. It was noted that the P30 Core Center Program has given NIEHS visibility and a broad national constituency. Other comments dealt with moving towards disease focus and regional Centers. The benefit for establishing regional Centers would be more efficient use of facilities; this would

be a potential strength to smaller institutions. Negative aspects would be the potential lack of face-to-face training opportunities, and loss of the ability of the current core facilities to buy access to institutional resources. Regional versus local Centers may impact leveraging. In conclusion, Council felt the report initiated debate on how to improve the Centers and suggested that the slides from the presentation be given to the Center directors.

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

XIII. CONSIDERATION OF APPLICATIONS

The Council considered 392 applications requesting $125,571,568 in total direct cost. The Council recommended 233 applications with the total direct cost of $81,098,170.

ADJOURNMENT OF THE NAEHS COUNCIL

The meeting was adjourned at 11:40 a.m. on February 15, 2005.