DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR RESEARCH RESOURCES

NATIONAL ADVISORY RESEARCH RESOURCES COUNCIL
MINUTES OF MEETING
MAY 20, 2004

The National Advisory Research Resources Council convened for its 127th session at 8:30 a.m. on Thursday, May 20, 2004, in Conference Room 10, Building 31. Dr. Judith L. Vaitukaitis, Director, National Center for Research Resources (NCRR), National Institutes of Health (NIH), presided as Chair. The meeting was open to the public until 2:00 p.m., at which time it was closed to the public for the review, discussion, and evaluation of grant applications as provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code, and Section 10(d) of Public Law 92-463.

COUNCIL MEMBERS PRESENT

Dr. Stephen W. Barthold
Dr. Robert J. Beall
Dr. Wah Chiu
Dr. Kenneth G. Cornetta
Dr. Randall E. Dalton
Dr. Mark H. Ellisman
Dr. Catherine C. Fenselau
Dr. James G. Fox
Dr. Joan S. Hunt
Dr. Gwen A. Jacobs
Dr. Cynthia E. Keppel
Dr. Thomas G. McGuire
Dr. Monte Westerfield
Ms. Sheila C. Zimmet
Dr. Stuart M. Zola
Dr. Roland F. Hirsch
Liaison Member, DOE

COUNCIL MEMBERS ABSENT

Colonel (Dr.) Peter Demitry
Dr. Eon Nigel Harris
Dr. John E. Maupin, Jr.
Dr. Paul G. Ramsey
Dr. Machi F. Dilworth
Liaison Member, NSF

SPECIAL INVITED GUESTS FOR OPEN SESSION

Dr. Nancy J. Brown, Associate Professor of Medicine and Pharmacology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN
Dr. David M. Eidelberg, Director, Center of Neuroscience, North Shore - Long Island Jewish Research Institute, New York University School of Medicine, Manhasset, NY
Dr. Gordon H. Williams, Professor of Medicine, Brigham and Women's Hospital, Boston, MA

STAFF OF OTHER NIH COMPONENTS

Dr. Eileen W. Bradley, CSR/NIH

Dr. John F. Connaughton, NIDDK/NIH
Dr. Arthur A. Petrosian, CSR/NIH
Dr. Pushpa Tandon, CSR/NIH
Dr. Margaret D. Snyder, OSA/OD/NIH
Dr. Jane A. Steinberg, NIMH

OTHERS PRESENT

Ms. Vicki L. Contie, Equals Three Communications, Bethesda, MD
Ms. Joanne S. Hawana, The Blue Sheet, Chevy Chase, MD
Mr. Steven E. Stocker, Equals Three Communications, Bethesda, MD

OPEN SESSION

I. Call to Order: Dr. Judith Vaitukaitis, Director, NCRR

Dr. Vaitukaitis welcomed Council members and guests to the 127th meeting of the National Advisory Research Resources Council. She announced that the following Council members would not be present: Colonel (Dr.) Peter Demitry, Dr. Machi Dilworth, Dr. Eon Nigel Harris, Dr. John Maupin, and Dr. Paul Ramsey. She introduced Dr. Kelly Garcia, who has been appointed as the new Department of Veteran Affairs ex-officio for Council, replacing Dr. William King. Four new members of the Council—appointed by Tommy Thompson, Secretary, Department of Health and Human Services (DHHS)—were introduced. They are:

- Dr. Kenneth G. Cornetta, Joe C. Christian Professor and Chairman, Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN
- Dr. Cynthia E. Keppel, University Endowed Professor of Physics, Hampton University, Hampton, VA; and Staff Scientist at the Thomas Jefferson National Accelerator Facility, Newport News, VA
- Ms. Sheila Cohen Zimmet, Director, Research Assurance and Compliance, Georgetown University, Washington, DC
- Dr. Stuart M. Zola, Director, Yerkes National Primate Research Center at Emory University, Atlanta, GA

II. Consideration of Minutes

The minutes of the Council meeting held on January 22, 2004, were approved as written.

III. Future Meeting Dates: Dr. Judith Vaitukaitis, Director, NCRR

The next Council meeting will be held on Thursday, September 9, 2004.

IV. Personnel Update: Dr. Judith Vaitukaitis, Director, NCRR

DHHS Personnel

Mr. Charles Havekost was appointed as the DHHS Chief Information Officer in April 2004. Mr. Havekost will oversee the DHHS information technology resources, program systems, and infrastructure. He also will be responsible for the development of enterprise architecture in compliance with the Office of Management and Budget's regulations and administration policy.

Dr. Bernard A. Schwetz was appointed as the director of the Office for Human Research Protections (OHRP) in April 2004. Prior to this appointment, Dr. Schwetz served as acting director of OHRP since February 2003, leading the Department's efforts to ensure the protection of human subjects in research.

NIH Personnel

Dr. Ann Hagan was named Associate Director for Extramural Activities (ADEA) at the National Institute of General Medical Sciences (NIGMS) in May 2004. Prior to this appointment, Dr. Hagan served as the Acting ADEA and the Deputy ADEA.

Dr. Timothy Condon was named Deputy Director of the National Institute on Drug Abuse in December 2003. In addition, he will continue to serve as Director of the Institute's Office of Science Policy and Communications.

NCRR Personnel

Dr. D. G. Patel transferred to the National Institute of Diabetes & Digestive & Kidney Diseases in February 2004. Dr. Patel was a Scientific Review Administrator in NCRR's Office of Review.

V. Legislative and Budget Updates: Dr. Judith Vaitukaitis, Director, NCRR

Dr. Vaitukaitis reported on the 2004 and 2005 NCRR Appropriation:

The FY 2004 Consolidated Appropriations Bill was passed by Congress and signed by the President on January 23, 2004. The total NCRR funding for FY 2004 is $1.2 billion, an increase of $40 million over FY 2003.

The President's budget request for the NCRR in FY 2005 is $1.1 billion, a decrease of $84.9 million, or 7.2 percent, below the FY 2004 Final Conference Level, due to the elimination of funding for the construction program.

Dr. Vaitukaitis also reported on the Reauthorization of NIH:

Congress has indicated that it plans to develop legislation to reauthorize NIH, which last occurred in 1993. On May 10, 2004, several Institute and Center directors met with congressional staff to discuss issues related to priority setting, the structure of NIH, the Roadmap, and grants funding.

VI. The Importance of NCRR-Supported Genotyping and Phenotyping Centers: Dr. Anthony R. Hayward, Director, Division for Clinical Research Resources, NCRR

Dr. Hayward discussed the importance of high-throughput genotyping centers. NCRR had released a Request for Applications to stimulate the establishment of cost-efficient centers that would make use of very sophisticated technologies. These applications have been reviewed, and NCRR expects to make an award in the summer of 2004. The proposed research to be conducted at these centers will expand the Nation's resources for high-throughput genotyping under conditions that allow for economies of scale, quality assurance, and data sharing. The centers will employ new approaches to identifying the associations between genotype and phenotype, leading to better understanding and improved treatment of various disorders.

VII. The Role of Pharmacogenetics in Therapeutic Decision Making - Facts and Fantasies: Dr. Gordon H. Williams, Professor of Medicine, Brigham and Women's Hospital

Dr. Williams discussed how genotyping and phenotyping could help in treating and preventing diseases. He described how an individual's genes interact with the environment to cause complex diseases. By knowing how they correlate, physicians can establish the appropriate therapy. The first step in studying complex diseases genetically is to consider them as syndromes and to document their traits. These traits should be much more prevalent in individuals with the disease in question versus those without. This entire process requires the identification of individual phenotypes (i.e., outward characteristics), which will later be used in a controlled environment such as a General Clinical Research Center (GCRC). Analyses of the genetics of hypertension illustrate the problems. Previous studies had been slowed by the diversity of hypertension, and it was only when patients could be separated into those who were, or were not, salt sensitive that the contributing haplotypes could be identified.

In the Brigham and Women's Hospital GCRC, Dr. Williams and his team were able to determine why some individuals with hypertension retain more salt than others. In a controlled environment, they monitored the salt intake of hypertensive patients, administered angiotensin II, and measured the aldosterone and renal blood flow responses. They found abnormal aldosterone and renal blood flow responses to angiotensin II due to genotype variations in the angiotensinogen and angiotensin converting enzyme (ACE) genes. By performing these studies in the controlled environment, they were able to determine that this group of hypertension patients should be treated with ACE inhibitors.

By continuing to perform genotyping and phenotyping in controlled environments, more therapeutic and preventive approaches to complex diseases can be achieved.

VIII. Brain and Behavior in Parkinsonism: Disease Progression and Therapy: Dr. David M. Eidelberg, Director, Center of Neuroscience, North Shore - Long Island Jewish Research Institute, New York University School of Medicine

Dr. Eidelberg discussed Positron Emission Tomography (PET) imaging of metabolic changes in the brains of patients with Parkinson's disease, and ways to correlate these metabolic changes with symptoms of the disease. By using appropriate radiolabeled compounds, PET imaging can show dopamine transport and glucose metabolism in the brain.

Symptoms of Parkinson's disease were measured in each patient by using the Unified Parkinson's Disease Rating Scale (UPDRS), and the symptoms were correlated with the PET images. Statistical analysis of many patients allowed the researchers to find patterns of changed activity in specific sections of the brain in Parkinson's disease patients. These patterns are called Parkinson's disease-related patterns (PDRP).

By using PET imaging to quantify PDRP activity and using the UPDRS to measure symptoms, the researchers were able to correlate metabolic changes in the brains of patients with the patients' disease symptoms. These techniques also allow the researchers to visualize the effects of treatments on the patients' brains and evaluate the effects on disease symptoms. This is a valuable method for comparing the relative efficacy of treatment methods, and for finding factors that influence the efficacy of treatments. Dr. Eidelberg noted that GCRCs are the ideal environment for this type of research because they bring research on imaging techniques together with rigorous clinical practices.

IX. Research Project Grants Interacting with Roadmap-Supported Technology Development Centers in a Hub and Spoke Model - Concept Clearance: Dr. Douglas M. Sheeley, Health Scientist Administrator, Division for Biomedical Technology Research and Research Resources, NCRR

Dr. Douglas Sheeley presented a concept to issue a solicitation for research project grants that will interact with Roadmap-Supported Technology Development Centers in a Hub and Spoke Model. He stated that NCRR is leading an NIH Roadmap effort to develop a network of National Technology Centers for Networks and Pathways (TCNPs) that will focus on the creation of new tools to describe the inherently dynamic interactions of proteins as quantitatively as possible. These centers will function as hubs of technology development, supporting—and, in turn, driven forward by—interactions with multiple research project grants supported by individual NIH institutes and centers.

As TCNP awards are announced, NIH institutes and centers will solicit research project grant applications from individual investigators who will work synergistically with the TCNPs to either extend the technological capabilities being developed, or more

commonly, to leverage a center's analytical tools to solve a challenging biomedical research problem. This model will allow substantial expansion of the impact of the centers, adding resources in a dynamic, tailored manner for collaboration without diminishing the center's focus on the core mission of technology development.

NIH Roadmap funds will not support these satellite grants. Individual institutes and centers will jointly issue a program announcement and take assignment as appropriate. It is anticipated that the R01 and R21/R33 funding mechanisms will be available through a single announcement published in the fall of 2004.

Council endorsed the concept as proposed.

X. Integration of Clinical Research Environments - Concept Clearance: Dr. Elaine S. Collier, Assistant Director, Division for Clinical Research Resources, NCRR

Dr. Elaine Collier presented a concept to integrate informatics and scalable computing across clinical research environments (i.e., GCRCs) to meet an objective set forth in the NCRR Strategic Plan. She cited several situations in which informatics has been successfully integrated in the clinical research environment, and she reported on the status of their progress. Dr. Collier then outlined what NCRR expected to have complete by 2010. This included the anticipation that the researchers' and clinical teams' expertise and experience would be amplified by informatics to: enable timely, optimal design of clinical studies and trials; exploit previous research data and results; determine the number of potential participants nationwide; automate entry of data at point of generation; permit online access to administrative, financial, research data—including medical images—at all times; automate adverse event reporting and regulatory paperwork generation and delivery; and provide online access to tools for management, analysis, querying at any time.

The various resources that could be used to help implement this objective include: the GCRCs; the Rare Diseases Clinical Research Network Data and Technology Center; the Biomedical Informatics Research Network; and NCRR's connection with NIH and Federal informatics programs.

The approaches included in this concept are to: integrate information support for clinical research; conduct pilot tests in GCRCs and minority-serving institutions' clinical research centers; create standards driven by needs of stakeholders and end users; and partner with healthcare informatics communities, government agencies, industry, and educational institutions.

Dr. Collier concluded her presentation by stating that the next steps would be to perform an inventory of current informatics resources, obtain input from end users regarding their needs, and analyze the information technology requirements.

Council endorsed the concept as presented.

XI. Expansion of BIRN to Other Model Systems: Dr. Michael T. Marron, Director, Division for Biomedical Technology Research and Research Resources, NCRR

Dr. Michael Marron presented a brief overview of the Biomedical Informatics Research Network (BIRN). The BIRN currently consists of three neuroscience testbeds (Mouse BIRN, Brain Morphometry BIRN, and Functional Imaging BIRN) and a coordinating center. Dr. Marron proposed to expand the BIRN testbeds to include more animal models of disease and development; increase the diversity of data types and scope to include organ systems and diseases outside of the central nervous system and animals other than mice; and expand development of tools for curation, storage, and retrieval, and data mining.

Council endorsed the concept as presented.

XII. Roadmap Initiatives and September 2004 Council: Dr. Louise E. Ramm, Deputy Director, NCRR

Dr. Louise Ramm presented an overview of the NIH Roadmap and how it was initially developed. The three overall themes of the Roadmap are: *New Pathways to Discovery*, *Research Teams of the Future*, and *Re-engineering the Clinical Research Enterprise.* All NIH Institutes and Centers are committed to investing jointly in a pool of resources to support current and future Roadmap initiatives.

Dr. Ramm indicated that, in September 2004, the Council will review applications submitted in response to the following Roadmap initiatives: *Exploratory Centers (P20) for Interdisciplinary Research* and *National Technology Centers for Networks and Pathways*. The Council will review these applications for all of NIH, as they are trans-NIH initiatives. Also, Council will review *National Centers for Biomedical Computing* applications for which NCRR has dual assignment.

CLOSED SESSION

This portion of the Council 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).

Council members discussed 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 that effect.

XIII. Application Review

Council considered 370 applications and recommended 370 for the total amount of $319,094,488.

ADJOURNMENT

The Council adjourned at 3:00 p.m. on May 20, 2004.

CERTIFICATION

We hereby certify that, to the best of our knowledge, the foregoing minutes and supplements are accurate and complete.

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Judith L. Vaitukaitis, M.D. Date
Chair, National Advisory Research Resources Council
and
Director, National Center for Research Resources, NIH

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Louise E. Ramm, Ph.D. Date
Executive Secretary, National Advisory Research Resources Council
and
Deputy Director, National Center for Research Resources, NIH

These minutes will be formally considered by the Council at its next meeting; corrections or notations will be incorporated into the minutes of that meeting.

Attachment:
Council Roster

NOTE: Open Session materials are available from the Executive Secretary or the Committee Management Office, NCRR.