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

NATIONAL ADVISORY RESEARCH RESOURCES COUNCIL
MINUTES OF MEETING
JANUARY 19, 2006

The National Advisory Research Resources Council (NARRC) convened for its 132nd session at 8:00 a..m. on Thursday, January 19, 2006, in Conference Room 10, Building 31. Dr. Barbara M. Alving, Acting Director, National Center for Research Resources (NCRR), National Institutes of Health (NIH), presided as Chair. The meeting was open to the public until 1:40 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. Robert J. Beall
Dr. Wah Chiu
Dr. Kenneth G. Cornetta
Dr. Randall E. Dalton
Dr. Machi F. Dilworth
Liaison Member, NSF
Dr. Mark H. Ellisman
Dr. Catherine C. Fenselau
Dr. James G. Fox
Dr. Kelly D. Garcia
Dr. Roland F. Hirsch
Liaison Member, DOE
Dr. Joan S. Hunt
Dr. Barbara B. Knowles
Dr. Bettie Sue Masters
Dr. Thomas G. McGuire
Dr. Arthur W. Toga
Ms. Sheila C. Zimmet
Dr. Stuart M. Zola

COUNCIL MEMBERS ABSENT

Col. (Dr.) Peter Demitry
Dr. Cynthia E. Keppel
Dr. John E. Maupin, Jr.
Dr. Paul G. Ramsey

SPECIAL INVITED GUESTS FOR OPEN SESSION

Dr. Carl A. Pinkert, Professor of Aging and Developmental Biology, University of Rochester School of Medicine and Dentistry
Dr. Julie W. Pan, Associate Professor, The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine
Dr. Story C. Landis, Director, National Institute of Neurological Disorders and Stroke (NINDS)
Dr. Thomas R. Insel, Director, National Institute of Mental Health (NIMH)
Dr. Bruce R. Rosen, Professor of Radiology and Health Sciences Technology, Harvard Medical School and Massachusetts General Hospital
Dr. Steven G. Potkin, Professor of Psychiatry and Human Behavior, University of California, Irvine School of Medicine

Dr. Peter R. MacLeish, Professor and Chairman of Anatomy and Neurobiology and Director of the Neuroscience Institute, Morehouse School of Medicine

STAFF OF OTHER NIH COMPONENTS

Dr. Sally A. Amero, CSR
Ms. Lora Kutkat, OD/NIH
Dr. Zehmy Li, CSR
Dr. Ross D. Shonat, CSR
Dr. Margaret D. Snyder, OER/OD/NIH

OTHERS PRESENT

Ms. Michelle R. Rodrigues, SRI International
Dr. Donna J. Dean, Lewis-Burke Associates, LLC
Mr. Stephen J. Heinig, Senior Staff Associate, Division of Biomedical and Health Sciences Research, Association of American Medical Colleges, Washington, D.C.

OPEN SESSION

I. Call to Order: Dr. Barbara M. Alving, Acting Director, NCRR

Dr. Alving welcomed Council members and guests to the 132nd meeting of the National Advisory Research Resources Council. She announced that the following Council members would not be present: Col. (Dr.) Peter Demitry, Dr. Cynthia E. Keppel, Dr. John E. Maupin, Jr., and Dr. Paul G. Ramsey.

II. Consideration of Minutes: Dr. Barbara M. Alving, Acting Director, NCRR

The minutes of the Council meeting held on September 15, 2005, were approved as written.

III. Future Meeting Dates: Dr. Barbara M. Alving, Acting Director, NCRR

The next Council meeting will be held on Thursday, May 18, 2006.

IV. Personnel Update: Dr. Barbara M. Alving, Acting Director, NCRR

NIH Personnel

Dr. Stephen I. Katz, Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, has been designated by NIH Director Dr. Elias A. Zerhouni to be the NIH liaison to the National Aeronautics and Space Administration (NASA). In this role, Dr. Katz will act as Dr. Zerhouni's principal representative and NIH point of contact for matters that concern both NASA and NIH.

V. Legislative and Budget Updates: Dr. Barbara M. Alving, Acting Director, NCRR

In FY 2005, NCRR funded 1,067 research grants, 69 research and development contracts (including loan repayment contracts), 134 full-time trainee positions, and 10 construction grants.

Dr. Alving reported on the FY 2006 NCRR Appropriation:

On December 30, the President signed into law H.R. 3010, the FY 2006 Labor, HHS, Education Appropriations Act. It appropriates $28.7 billion for NIH, an increase of $107 million over the FY 2006 request, and an increase of $206 million over the comparable FY 2005 budget. However, $100 million of that appropriation will be transferred to the Global HIV/AIDS account. The total net funding for NCRR, after an across-the-board reduction of 1 percent for all discretionary spending, is $1.089 billion, which excludes $9.8 million to be transferred out for Roadmap activities. The conference agreement, after the 1 percent reduction, provides $323 million from NCRR and NIH Roadmap funds for the General Clinical Research Centers and the Clinical and Translational Science Awards combined. It also provides $220 million for the Institutional Development Award program. No funds were appropriated for NCRR's Research Facilities Improvement (C06 Construction) Program.

Dr. Alving also reported on the new NIH Office of Portfolio Analysis and Strategic Initiatives (OPASI), established by Dr. Zerhouni to ensure a coordinated assessment and management of the overall portfolio of NIH-funded research. OPASI will help to identify important areas of emerging scientific opportunities and assist in accelerating investments in these areas, focusing on those that involve multiple NIH Institutes and Centers.

VI. Updates on Upcoming NCRR Workshops: Dr. Harold L. Watson, Health Scientist Administrator, NCRR; Dr. John (Jack) D. Harding, Director of the Primate Resource Program, Division of Comparative Medicine, NCRR; Dr. Michael H. Sayre, Health Scientist Administrator, NCRR; Dr. Peter T. Highnam, Senior Advisor to the Director, NCRR

Dr. Alving introduced four brief presentations on upcoming NCRR workshops. These workshops stem from the NCRR FY 2007 Budget Retreat, held in August 2005.

<u>Navigating the Translational Researcher Through a Complex of Animal and Biological Resources</u>

Dr. Watson reported that this workshop, scheduled for March 6-7, 2006, will consider the creation of a comprehensive resource portal that researchers can use to find and effectively utilize all NIH-supported animal model and related biological resources. This portal, or Animal Information Center, would enhance access and retrieval of information from existing model databases and accommodate the addition of new model databases.

Workshop participants will identify the portal user community and its needs, determine the nature and ideal characteristics of the resource, describe the range of expertise needed to staff and support the resource, and ensure that this translational resource will evolve in concert with the science and technology that it provides.

Genetic Tools for Optimizing the Use of Rhesus Macaques for Translational Research

Dr. Harding noted that NCRR-funded investigators have recently developed genetic/genomic tools, such as genetic maps and microarrays, that should greatly facilitate the further development of the rhesus as an animal model for human disease. This workshop, scheduled for April 19-20, 2006, will define the next generation of genetics-based tools to facilitate the use of the rhesus macaque in translational research. Workshop presentations will summarize existing rhesus-specific genetics tools, and panels of experts in application areas—such as AIDS and other infectious diseases, biodefense, and neurobiology—will define needs specific to those disciplines.

Supporting Connectivity for Biomedical Research

Dr. Sayre noted that this half-day workshop, to be held April 24, 2006, will explore ways to partner with other agencies, academic organizations, and the private sector to further expand and optimize investments in computer network connectivity to support health-related research. Representatives from NCRR-supported basic and clinical research centers and research resources will be invited to meet with high-level networking and information technology experts from industry, government, and academia. The goal of the workshop will be to produce a strategic plan to maximize the power of connectivity among NCRR grantees and the communities they serve and identify strategic partnerships to share costs where mutual interests exist.

Ensuring the Inclusion of Clinical Research in the National Health Information Network

Dr. Highnam noted that the goal of this meeting, to be held in May 2006, is to lay the groundwork for a plan to include clinical and translational research in the National Health Information Network (NHIN), which currently focuses exclusively on healthcare. This meeting—jointly organized by the NCRR, the Agency for Healthcare Research and Quality, and FasterCures—will highlight opportunities to enable faster discovery and verification of treatments and cures via NHIN and commercial electronic health records systems.

VII. NIH Blueprint for Neuroscience Research: Dr. Thomas R. Insel, Director, National Institute of Mental Health (NIMH), and Dr. Story C. Landis, Director, National Institute of Neurological Disorders and Stroke (NINDS)

Dr. Insel noted that diseases of the nervous system represent a significant public health problem that affects one in three Americans. Because these diseases are so wide-ranging—spanning the life cycle and impacting multiple organ systems—NIH Director

Dr. Elias Zerhouni proposed that this health issue would best be addressed through a collaborative effort involving multiple NIH components and researchers from a variety of disciplines. Therefore, in 2004, NIH launched the Blueprint for Neuroscience Research, a trans-NIH initiative involving 16 NIH Institutes and Centers and jointly led by NINDS and NIMH.

One project initiated during the NIH Blueprint's first year is the development of graduate-level academic courses on the neurobiology of disease. The courses, which address pathology and basic underlying science, are designed to increase cross talk between clinical and basic investigators and their departments. Another Blueprint project, known as the Neuroscience Information Framework, is developing an extensive Web-based "database of databases" that will serve as a centralized access point for a broad range of neuroscience-related data.

The NIH Blueprint is now in the process of rolling out initiatives for 2006 and planning new initiatives for 2007. Among the initiatives to be launched this year are Interdisciplinary Center Cores, which will provide resources and facilities for neurobiology research and will encourage interactions and collaboration among neuroscientists in different departments, disciplines, and institutions. The NIH Blueprint is also expanding the scope of its neuroscience training programs to include courses in computational neuroscience and in neuroimaging. Another new effort for 2006 will enhance the study of behavior—an important component of many nervous system disorders—by establishing uniform measures of cognitive, sensory, and motor functions. This initiative, called the Toolbox for Assessment of Neurological and Behavioral Function, will develop tools that enable comparisons and data compilation across studies, thereby enriching epidemiological and population-based studies. In future years, the NIH Blueprint will focus on specific themes: neurodegeneration in 2007, nervous system development in 2008, and neural plasticity in 2009.

VIII. Overview of the Biomedical Informatics Research Network (BIRN): Dr. Bruce R. Rosen, Professor of Radiology and Health Sciences Technology, Harvard Medical School and Massachusetts General Hospital

Dr. Rosen explained that BIRN involves a consortium of 28 research institutions and 37 research groups participating in a wide variety of projects involving brain imaging of human neuropsychiatric disease and associated animal models. Some groups are working on large-scale, cross-institutional imaging studies on Alzheimer's disease, schizophrenia, and depression using structural and functional magnetic resonance imaging (MRI). Others are studying animal models relevant to multiple sclerosis, attention deficit disorder, and Parkinson's disease using MRI, whole-brain histology, and high-resolution light and electron microscopy. These projects present practical and immediate requirements for performing large-scale biomedical informatics studies and provide multiple usage cases for distributed computation and the handling of heterogeneous data. Incorporation and harmonization of multiple neuro-ontologies across datasets, which are critical for the long-range goal of data mining through this infrastructure, is just one of the many

practical issues addressed by BIRN.

Every day, scientists connected by BIRN are working with their colleagues across the country to develop and refine imaging and analytic tools that can be used for multisite data integration. BIRN tools are available to researchers around the world as they pursue the causes of Alzheimer's disease, schizophrenia, major depression, attention deficit hyperactivity disorder, and autism, and develop effective treatments. Researchers in other medical fields, including cardiology and cancer, recognize the value these tools have to their research and their wide applicability throughout biomedical research.

BIRN uses emerging technology advances to enhance collaborative efforts that integrate data, expertise, and unique technologies from research centers across the country. The first three years of the project have led to significant contributions with the promise of further development and wider applicability. Accomplishments include making publicly available tools and datasets, as well as building network infrastructure. Large-scale collaborations are dependent on the capabilities of the national cyberinfrastructure of high-speed networks, distributed high-performance computing, and the necessary software and data integration capabilities. However, these technologies are changing rapidly—in part—because of how they are being used by large biomedical projects. Thus, collaborations within BIRN include scientists in a large number of biomedical sub-disciplines as well as computer scientists and engineers who are creating this cyberinfrastructure.

IX. BIRN Coordinating Center: Dr. Mark H. Ellisman, Professor of Neurosciences and Bioengineering, University of California, San Diego

Dr. Ellisman discussed the development and deployment of key infrastructure components for immediate and long-term support of the scientific goals pursued by biomedical scientists. These components include high-bandwidth, inter-institutional connectivity; a uniform security model; and grid-based file management and computational services. Software and techniques have been developed to federate data and databases, as well as to increase data handling performance and resiliency. This infrastructure enables shared processing and visualization.

As a core component of the BIRN infrastructure, Internet2 provides a solid foundation for the future expansion of the infrastructure, as well as the stable high-performance network required by researchers in this national collaborative project. Internet2 is the US consortium—led by over 200 universities working in partnership with industry and government—that is leading the way to develop and deploy advanced network applications and technologies. Researchers are also benefitting directly from the connectivity to high-performance computing resources, such as TeraGrid. The National Science Foundation (NSF) launched the TeraGrid in 2001 to exploit grid technologies that provide integrated, persistent, leading-edge computational resources for researchers. Today, the TeraGrid serves resources from eight partner supercomputing sites across the country. BIRN testbed researchers from multiple sites have recently used the BIRN and

TeraGrid resources to perform computationally demanding advanced-shape analyses of anatomical structures in the brain in order to better characterize specific disorders.

The requirements of the biomedical community are evolving through experience with large biomedical computation projects. At the same time, the nationwide cyberinfrastructure being assembled to enable large-scale science projects also will evolve. The BIRN program is uniquely situated to serve as a major bidirectional conduit between the biomedical research community of NIH-sponsored programs and the information technology development programs, mostly supported by other government agencies and by industry.

X. Morphometry BIRN: Dr. Bruce R. Rosen, Professor of Radiology and Health Sciences Technology, Harvard Medical School and Massachusetts General Hospital

Dr. Rosen described the scientific goals, methods, preliminary results, and long-term vision for the Brain Morphometry BIRN (mBIRN). The overall goal of the mBIRN is to develop the capability to collect, analyze, and mine data acquired at multiple sites—while using processing and visualization tools developed at multiple sites—to study the neuroanatomical correlates of neuropsychiatric illnesses. Through large-scale analyses of patient population data acquired and pooled across sites, mBIRN scientists are investigating whether brain structural differences correlate to symptoms such as memory dysfunction or depression, and whether specific structural differences distinguish diagnostic categories.

The mBIRN effort is divided into four broad categories: calibration; analysis and visualization; computational informatics; and utilization. The mBIRN has developed and validated procedures that allow data to be acquired on multiple vendor platforms, at multiple time points, to be analyzed as a single dataset. Current efforts involve working to extend this paradigm to a broad variety of imaging techniques. Working with the BIRN Coordinating Center, investigators at different sites have developed integrated data analysis and visualization tools to process clinical data in unique ways, and application of informatics tools has allowed mBIRN investigators to make fundamental new discoveries on the relationships between brain anatomy and clinical symptoms. Several mBIRN developments have been adopted and utilized by investigators in Function and Mouse BIRN and by other national consortium groups throughout the country.

XI. Function BIRN: Dr. Steven G. Potkin, Professor of Psychiatry and Human Behavior, University of California, Irvine School of Medicine

Dr. Potkin discussed what many considered improbable just a few years ago: the ability to perform multisite functional imaging studies on the most vexing neuropsychiatric diseases and disorders affecting mankind. Measures of brain activities involved in thinking and emotion are by their very nature subtle, and functional imaging measurements are not made in the same ways in different centers at different locations. Therefore, calibration across sites is important, because brain scans from a single individual can appear

markedly dissimilar when collected using different MRI instruments. To that end, FBIRN has developed methods of standardization and calibration to reduce variability between sites—a major breakthrough for multisite imaging studies.

To share these techniques, FBIRN has developed a distributed infrastructure that includes standardization protocols, a human imaging database, quality assurance methods, and protection of subject confidentiality. Coupled with improved methods for three-dimensional alignment of brains for accurate comparisons and automated image-analysis pipelines, these developments will rapidly create the required and unusually large datasets critical to understanding the subtlety of schizophrenia and other neuropsychiatric diseases and brain disorders. FBIRN is developing new cognitive tasks that tap the important interaction between cognition and emotion, cutting-edge methods for image analysis and display, and new methods to further reduce variation among sites.

XII. Mouse BIRN: Dr. Arthur W. Toga, Professor of Neurology at the University of California, Los Angeles School of Medicine

Dr. Toga provided an overview of the objectives, status, and scientific applications of the Mouse BIRN. Its goals are to develop tools that enable sharing and mining of multiscale structural and functional mouse brain data. An enormous worldwide effort to understand the relationship between mouse genotype, phenotype, and behavior is currently underway. Numerous studies collect data about genes and their expression in the mouse, including many specifically constructed mouse strains that model diseases that affect humans. Currently, there is no real infrastructure to share data and compare observations—about gene expression, neuroanatomy, or other variables—within a quantitative and visual framework. The focus of the Mouse BIRN is to create and distribute such a capability.

Building upon considerable progress from previously independent groups, Mouse BIRN scientists have created an integrated, networked system that maps data from different animals, different data types (at different scales), and from multiple laboratories into a unified measurement and display package. Data can be distributed or remain local. The package includes image and data manipulation tool sets to make data comparable. Also, the package is adaptable and extensible, accepting new modules that identify structures, (i.e., new anatomic templates). Mouse BIRN scientists have collected and created a database of high-field magnetic resonance data, histology, gene expression, and other data describing the mouse brain. The scientists also have identified three disease model test beds (Alzheimer's disease, multiple sclerosis, and Parkinson's disease) to evaluate the infrastructure.

XIII. The Neuroscience Institute at Morehouse School of Medicine: Dr. Peter R. MacLeish, Professor and Chairman of Anatomy and Neurobiology and Director of the Neuroscience Institute, Morehouse School of Medicine

Dr. MacLeish discussed the creation and development of the Morehouse School of Medicine's Neuroscience Institute, established in 1994. The institute provides

opportunities for faculty and students to explore the workings of the nervous system and to develop potential treatments for neurological and psychiatric disorders, particularly those that disproportionately affect minority populations. An important component of the Neuroscience Institute involves the training of minority researchers, which will help to increase the Nation's workforce of well-trained biomedical scientists. Training opportunities include summer research programs for undergraduate and medical students, graduate training, and undergraduate course work.

Today, the Neuroscience Institute comprises three research program areas (stroke, neuroprotection and repair, and sleep and circadian rhythm) and has two new core facilities, specializing in imaging and genomics. Six new NIH research project (R01) grants have been secured under the umbrella of the Neuroscience Institute, including a project that identified a gene important to motor neuron function and another that identified a neuroprotective molecule that shows promise for the treatment of stroke. In addition, the institute is engaged in a broad NIH-funded effort to develop a stroke prevention and intervention research program, which covers the range from basic science to population-based studies.

Morehouse's Neuroscience Institute receives primary funding from the National Institute of Neurological Disorders and Stroke and builds on the strength of the university's enhanced research capacity, fostered by NCRR's Research Centers in Minority Institutions Program and other NIH programs. In addition, the institute has benefitted from creating productive partnerships with other Federal and private agencies.

XIV. Council Operating Procedures: Dr. Louise Ramm, Deputy Director, NCRR

Dr. Ramm reported two minor modifications to the Council Operating Procedures: 1) The procedures were modified to reflect changes in the closed session; rather than breaking out into two panels, the entire Council will remain together in the room. 2) The mechanism by which Council members are asked to participate in the early concurrence has been modified.

The Council Operating Procedures were accepted as modified.

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.

XV. Application Review

The Council considered 255 applications and recommended 255 for a total first-year amount of $105,730,762 (direct costs).

ADJOURNMENT

The Council adjourned at 3:30 p.m. on January 19, 2006.

CERTIFICATION

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

Barbara Alving

Dr. Barbara M. Alving
Chair, National Advisory Research Resources Council
and
Acting Director, National Center for Research Resources, NIH

3/13/06
Date

Louise Ramm

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

3/13/06
Date

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.