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

NATIONAL ADVISORY RESEARCH RESOURCES COUNCIL
MINUTES OF MEETING
MAY 17, 2001

The National Advisory Research Resources Council (NARRC) convened for its 118th session at 9:15 a.m. on Thursday, May 17, 2001, in Conference Room 10, Building 31. Dr. Louise E. Ramm, Deputy Director, National Center for Research Resources (NCRR), National Institutes of Health (NIH), presided as Chair for the morning session. The meeting was open to the public until 2:30 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. Joseph D. Andrade
Dr. Stephen W. Barthold
Dr. Kenneth I. Berns
Ms. Catherine D. Bertram
Dr. Robert J. Desnick
Dr. Chien Ho
Dr. Gwen A. Jacobs
Dr. Peter O. Kohler
Dr. Evangelia G. Kranias
Dr. William R. Morton
Dr. Diana S. Natalicio
Dr. Judith L. Swain
Dr. Burton A. Weisbrod
Dr. Monte Westerfield
Dr. Machi F. Dilworth
Liaison Member, NSF
Lt Col Alfred S. Graziano Jr., USAF
Ex-Officio, DOD
Dr. Roland F. Hirsch
Liaison Member, DOE
Dr. William W. King
Ex-Officio, VA

COUNCIL MEMBERS ABSENT

Dr. Eon Nigel Harris
Dr. Michael M.E. Johns
Dr. Peter A. Kollman
Dr. James H. Wyche

SPECIAL INVITED GUESTS FOR OPEN SESSION

Dr. Sally S. Atherton, Professor and Chair, Department of Cellular Biology and Anatomy, Medical College of Georgia, Augusta, Georgia
Dr. Richard A. Galbraith, Program Director, General Clinical Research Center, University of Vermont, Burlington, Vermont
Dr. James E. Heubi, Professor of Pediatrics, General Clinical Research Center, Children's Hospital Medical Center, University of Cincinnati School of Medicine, Cincinnati, Ohio

Dr. M. Louise Markert, Program Director, General Clinical Research Center, Duke University Medical Center, Durham, North Carolina
Dr. Tilahun D. Yilma, Director and Professor of Virology, International Laboratory of Molecular Virology for Tropical Disease Agents, School of Veterinary Medicine, University of California, Davis, California

STAFF OF OTHER NIH COMPONENTS

Dr. Marjam Behar, CSR/NIH
Dr. John Bowers, CSR/NIH
Dr. Mark Guyer, NHGRI/NIH
Dr. Nancy Lamontagne, CSR/NIH
Dr. Jane Petersen, NHGRI/NIH
Dr. Arnold Revzin, CSR/NIH
Dr. Eugene Vigil, CSR/NIH

OTHERS PRESENT

Ms. Adwoa Boahene, *The Blue Sheet*, Chevy Chase, Maryland
Dr. Roger Bumgarner, Research Assistant Professor, Microbiology, University of Washington, Seattle, Washington
Dr. T. J. Dunlap, JTxCo, Texas
Dr. Michael Katze, Associate Director of Research, Regional Primate Research Center, University of Washington, Seattle, Washington
Mr. Steve Heinig, Senior Staff Associate, Division of Biomedical and Health Sciences Research, Association of American Medical Colleges,Washington, DC
Ms. Nancy Moy, SRI International, Menlo Park, California

OPEN SESSION

I. Call to Order
Dr. Louise Ramm, Deputy Director, NCRR

Dr. Ramm welcomed NARRC members and guests to the 118th meeting of the NARRC. She announced that the following Council members would not be present: Dr. Eon Nigel Harris, Dr. Michael Johns, Dr. Peter Kollman, and Dr. James Wyche. She introduced three new Council members: Dr. Stephen W. Barthold, Professor of Pathology and Director of the Center for Comparative Medicine, School of Veterinary Medicine, University of California, Davis; Dr. Gwen A. Jacobs, Associate Professor of Neuroscience in the Department of Cell Biology and Neuroscience and Co-Director of the Center for Computational Biology, Montana State University; and Dr. Monte Westerfield, Professor of Biology and Director of the Zebrafish International Resource Center, Institute of Neuroscience, University of Oregon.

II. Consideration of Minutes

The minutes of NARRC meeting held on January 18, 2001, were approved as written.

III. Future Meeting Dates

Dr. Ramm announced that the next NARRC meeting will be held on Thursday and Friday, September 13 and 14, 2001. A one-day meeting is being considered, and Council members will be notified of the decision.

IV. Personnel Update

Tommy G. Thompson became the Secretary of Health and Human Services (HHS) on February 2, 2001. Secretary Thompson has dedicated his professional life to public service, most recently serving as Governor of Wisconsin since 1987. As Secretary of HHS, his agenda includes plans to: modernize Medicare; enact a patient's bill of rights; provide access to affordable health insurance for the uninsured; continue welfare reform; take a leadership role in women's health; support biomedical research; and continue vigilant protection of the safety of the nation's food and drug supply.

NIH Acting Director Dr. Ruth Kirschstein has appointed Dr. Donna Dean as Acting Director of the newly established National Institute of Biomedical Imaging and Bioengineering (NIBIB). Dr. Dean has served as Dr. Kirschstein's special advisor for the past three years. Dr. Dean played a lead role in implementing last fall's legislative establishment of NIBIB. NIH is currently conducting a search for the new institute's first permanent director.

On May 16, NCRR Director Dr. Judith Vaitukaitis announced that the search for a new associate director of the Division of Clinical Research has been completed and it is anticipated that the selected candidate will fill the position in September 2001.

V. Division of Research Infrastructure Program Guidelines and Construction Grant Guidelines

Dr. Sidney McNairy, Jr., Associate Director, Division of Research Infrastructure, NCRR

Dr. McNairy presented the revised guidelines for programs administered by the Division of Research Infrastructure (DRI). He highlighted proposed guideline modifications for the Research Centers in Minority Institutions (RCMI) Program, the Science Education Partnership Award (SEPA) Program, as well as the Research Facilities Improvement Program (RFIP). A draft copy of the modified guidelines had been previously provided to Council members. Dr. McNairy discussed only those changes he thought were of significant interest to the Council.

He indicated that the recommended changes are based on a report by the Government Accounting Office; an evaluation of the RCMI Program; information provided by members of the NIH community and NCRR staff; and information gleaned from a review of existing NIH

Requests for Applications (RFAs) and Program Announcements (PAs). Dr. McNairy enumerated the recommendations and explained that the guideline modifications would help DRI to more clearly focus on the intent of each program.

Council unanimously approved the guidelines as modified.

VI. Report on the Establishment of the National Institute of Biomedical Imaging and Bioengineering (NIBIB)
Dr. Michael Marron, Associate Director, Division of Biomedical Technology (DBT), NCRR

Dr. Marron said NIBIB was established through Public Law 106-580. He reviewed the legislative process that founded NIBIB and highlighted its mission "...to improve health by promoting fundamental discoveries, design and development, and translation and assessment of technological capabilities."

NIBIB will support biomedical imaging and bioengineering research and training through existing and novel funding approaches; partner with NIH institutes and centers (ICs) to translate fundamental discoveries into research and applications; coordinate with other government agencies to translate technological developments into biomedical applications; and support the development of relevant standards and guidelines.

In Fiscal Year (FY) 2001, Congress did not appropriate funding for NIBIB, but $40 million has been proposed for FY 2002. During the startup phase of the new institute, grants and appropriate funds will be transferred from existing NIH ICs. Dr. Marron said that NCRR will transfer R01 and R21 (non-competing) grants, estimated to be about $6 million, to NIBIB. These project grants support biomedical imaging device development, biomaterials, biosensors, and nanotechnology. Initially, NCRR will assist NIBIB to administer these grants. Moreover, at their September meetings, the advisory councils for the ICs will review grants that are dually assigned to the ICs and NIBIB.

Several NARRC members suggested that Dr. Dean, the Acting Director of NIBIB, speak at a future NARRC meeting.

VII. Concept Clearance: Integrated Centers for Proteomics Research
Dr. Douglas Sheeley, Health Scientist Administrator, Division of Biomedical Technology, NCRR

Dr. Sheeley presented a concept to establish Integrated Centers for Proteomics Research. He defined proteomics as the study of the proteins expressed by the genome, and he emphasized that the proteome is difficult to study because it is dynamic–unlike the "static" genome. To address the technological complexities of understanding the proteome, the proposed centers would integrate cross-discipline expertise with multiple new and complementary technologies, techniques, and approaches–including bioinformatics. The technological research at these centers would be carried out within the context of a biological problem. The

centers would focus on systems-based, biochemistry approaches to ask either broad or strictly defined core questions about the proteome. Areas to be addressed include: protein expression and association; intracellular protein (protein interactions in both healthy and diseased states); space-time differences in the levels of gene expression; and post-translational modifications of proteins.

Dr. Sheeley noted that "post-genomic era" implies that certain information is accessible to be exploited. However, the scientific community cannot fully benefit from such information until difficult technological and methodological barriers are overcome. Dr. Sheeley noted important advances in mass spectrometry that have occurred over the past 20 years. Enabling the proteomic era, however, will require new technologies and approaches that progress beyond mass spectrometry to encompass a broader focus. In addition, mass spectrometry must be integrated more fully with separation science if one is to fully address complex samples. Moreover, new computational tools must be developed so the large data sets generated by mass spectrometry may be rendered as useful information.

Dr. Sheeley concluded his presentation by stating that NCRR plans to provide funding opportunities for the proposed centers by issuing a Request for Applications and utilizing the P41 grant mechanism to provide support.

Council endorsed the concept as presented.

VIII. Update on Chimpanzee Management Program (ChiMP) Working Group
Dr. John Strandberg, Associate Director, Division of Comparative Medicine, NCRR

Dr. Strandberg reported on the activities of the NARRC ChiMP Working Group, which advises NCRR on: the maintenance and use of chimpanzees; principles of colony management; database development; genetic monitoring; facilities construction or modernization; and mechanisms for ChiMP funding. The Working Group also establishes and evaluates criteria and policies for transferring ownership of chimpanzees from other sources to NIH and for possible divestiture of chimpanzees if overcrowding or a surplus occurs. Additionally, the group determines if the animals are more suitable for long-term housing at a sanctuary.

On May 16, 2001, the ChiMP Working Group met to discuss the care and management of chimpanzees that are owned by NIH. Currently, NCRR supports three ChiMP research facilities located at University of Texas in Bastrop; Primate Foundation of Arizona in Mesa; and University of Louisiana at Lafayette in New Iberia.

NCRR also will soon support a fourth facility, located in Alamogordo, New Mexico, to house approximately 250 chimpanzees–used in HIV and hepatitis research–that were recently titled from The Coulston Foundation to NIH. In addition, NCRR will provide support for a centralized database, the International Species Identification System (ISIS).

At the meeting of the ChiMP Working Group, Dr. O'Neill presented information from a recent search of the NIH CRISP database that identified 71 research grants that mentioned use of chimpanzees. However, several grants supported studies of genetics and not studies that used live chimpanzees. Most of the research dealt with hepatitis viruses–specifically, hepatitis C. The chimpanzee has been essential in developing the hepatitis B vaccine, and efforts are now focused on hepatitis C. An NIAID researcher presented a tiered and sequential approach that would reduce the number of chimpanzees needed in biomedical research.

After the presentations, the working group was consulted for advice on three issues:

- First, the research animal population must be evaluated to determine which animals are surplus and available for placement in a sanctuary and which animals should be kept in long-term housing for future use. Local and national needs must be considered.

- Second, a limited survey of existing facilities could help to estimate the number of chimpanzees required for pending short- and long-term research projects. Publicly and privately funded research needs for chimpanzees should be assessed, and the number and type of chimpanzees could be identified for potential housing in a sanctuary.

- Third, the process of determining which investigators receive priority access to these animals must be based on existing meritorious research funding.

Other Working Group discussion included the Interagency Animal Models Committee and comparative chimpanzee genomics. The Working Group plans to continue its meetings in conjunction with the NARRC meetings.

IX. Update on Chimpanzee Sanctuary Legislation
Dr. John Strandberg, Associate Director, Division of Comparative Medicine, NCRR

Dr. Strandberg reported on the status of activities related to the Chimpanzee Health Improvement, Maintenance, and Protection Act, which became Public Law 106-551 in December 2000. The Act stipulated that within 180 days the Secretary of Health and Human Services would establish a system to provide for the lifetime care of chimpanzees that have been used, or were bred, or were purchased for use in research conducted or supported by NIH, FDA, or other Federal agencies. On April 5, 2001, DHHS delegated the responsibilities set forth in the Act to NIH, providing authority for NIH to act on behalf of DHHS. Hence, NCRR's Division of Comparative Medicine, which has administered the NIH Chimpanzee Management Program since 1998, will establish the sanctuary system through competitive contract(s). NCRR expects to award contract(s) in FY 2002.

Prior to receiving DHHS authority to act on the provisions of the legislation, NCRR placed announcements in both the *Commerce Business Daily* and the *Federal Register*. These announcements requested private, nonprofit organizations to respond by May 15, 2001, if interested in serving as a contractor to NIH to establish a chimpanzee sanctuary.

Dr. Strandberg said that NCRR also has established an Advisory Working Group that will assist NCRR to set standards for operating a sanctuary system. The composition of the Working Group ranges from members who are veterinarians and animal-rights advocates to chimpanzee behaviorists and advocates for use of research animals.

NCRR has determined that approximately 200 animals are currently available to be housed in a sanctuary system. Many of these animals are old, in declining health, and possibly infected, which presents a separate set of husbandry concerns.

X. Report on Nonhuman Primate Genomics Workshop and Summary of Recommendations Dr. Jerry Robinson, Director of the Regional Primate Research Centers Program, Division of Comparative Medicine, NCRR

Dr. Robinson reported on the Nonhuman Primate Genomics Workshop sponsored by the University of Washington Regional Primate Research Center (RPRC) and held on January 22 and 23, 2001 in Seattle. Since many genetic similarities exist between the nonhuman primate (NHP) and the human, advanced genetic technologies are needed to maximize the use of this animal model to understand human health and disease. Therefore, the Workshop participants met to assess the current state of primate genomics; identify similar approaches and technologies from the Human Genome Project that could be applied to NHP models; and make recommendations for genome database development and technology resources to aid in NHP research.

The group recommended the following: developing bacterial artificial chromosome (BAC) libraries and cDNA libraries from 8 to10 tissue types from various developmental stages of the rhesus macaque, baboon, and chimpanzee; using various techniques to map genes on the chromosomes–such as radiation hybrid maps that help complement what some of the other genetic linkage maps can provide; and, after the libraries are established, the 8 to10 tissue types from the three animal models be sequenced and a shotgun approach be used to sequence the rhesus monkey genome. A large sequencing center would be required.

The group also recommended that bioinformatics resources be developed at the RPRCs. These resources would be specialized databases of genome information for personnel to annotate NHP information–DNA sequences, genome maps, and expression array data.

These recommendations are intended to help formulate future NCRR and NIH initiatives. Already, however, NCRR and the National Human Genome Research Institute (NHGRI) are planning to solicit applications for BAC library productions. Also, NCRR and the National Institute of Allergy and Infectious Diseases plan to request applications for microarray development and specific gene sequencing.

Following Dr. Robinson's presentation, Council members echoed the need for NCRR to take the lead in developing NHP sequencing activities across NIH and for a trans-NIH committee

to coordinate efforts in primate genomics. It was mentioned that the NHGRI is planning a July workshop to develop guidelines and criteria to be used in determining which organisms will be sequenced next.

XI. Recommendations to General Clinical Research Centers (GCRCs) for Research Subject Safety in Clinical Research

Dr. M. Louise Markert, Program Director, General Clinical Research Center, Duke University Medical Center

Dr. Markert presented the General Clinical Research Center (GCRC) Program Directors (PD) Association Committee's recommendations to GCRCs for research subject safety in clinical research. The Committee concluded that GCRCs should take a leading role to provide investigators and staff with education and training in several areas involving clinical research focusing on research subject safety. Recommendations in the areas of education, training, and support were addressed.

The committee recommended that investigators address data and safety monitoring issues for all GCRC protocols. It was recommended that each GCRC protocol have a data and safety monitoring plan. The plans will include adverse event (AE) reporting and periodic review as appropriate for each study. These plans should be approved by the GCRC Advisory Committee (GAC) prior to the initiation of the study. The minimum required content of the plan includes AE grading and attribution scale; plan for unanticipated AE reporting; plan for annual reporting of AEs; and plan for safety review.

The GAC may also require additional information if the study includes safety review questions, enrollment and protocol violations, or a plan for ongoing review of results.

AE reporting as defined by the Code of Federal Regulations requires investigators to report any "unanticipated problems involving risks to subjects" to the Institutional Review Board, and it also requires sponsors of protocols run under an Investigational New Drug Application (IND) with the FDA to notify the FDA of any event that is "both serious and unexpected." The Committee recommends that each GAC establish a procedure to review the expedited reports and that the GAC should establish a procedure to review the annual summary of AE for all protocols. Furthermore, the committee recommends that each GAC develop a mechanism to ensure that GCRC staff are provided education on the regulations involving AE reporting.

Regarding the areas of security and privacy, the PD Committee recommends that GCRCs follow the new regulations under the Health Insurance Portability and Accountability Act of 1996. Investigators must pay attention to privacy issues with respect to informed consent documents. The investigator also must be aware of and comply with regulations of the Joint Commission on Accreditation of Healthcare Organizations which requires a description in the medical chart that the informed consent process was completed.

Dr. Markert then discussed compliance with the Clinical Laboratory Improvement Act (CLIA). The CLIA requires certification of laboratories that report patient test results back to the patient or referring physician. CLIA regulations require research laboratories to be CLIA certified if any data from research or other testing on research patients are shared with physicians, counselors, or the patient or patient's family. All GCRC investigators should be informed of this requirement.

Drugs or biologics given to patients may be prepared under the auspices of an IND to the FDA or other national regulations. It is important that these materials be prepared under appropriate standards such as the FDA's Good Manufacturing Practices. The Committee recommends that if a GCRC investigator requests to administer biologics or drugs not approved by the FDA, the GAC should review laboratory procedures. The GAC may recommend that audits be performed by individuals external to the laboratory.

Dr. Desnick recommended that all new Research Subject Advocates (RSAs) at the GCRCs receive training at the annual PD meeting. In addition, an RSA working session could be held at the PD meeting to provide RSAs an opportunity for other education and to share experiences.

Council concurred with the recommendations.

XII. Budget Update
Dr. Judith L. Vaitukaitis, Director, NCRR

Dr. Vaitukaitis reported on FY 2002 Congressional Appropriations and also summarized NCRR program activities. She said that the President's FY 2002 budget requested $23.1 billion for NIH. This represents an unprecedented single-year increase of 12 to 13 percent. However, language in this budget states that in FY 2004 the President's request will be only a 2.8 percent increase for NIH.

For FY 2002, the President's budget requests $974 million for NCRR. This would represent an increase of approximately 19 percent over the FY 2001 funding level. Each NCRR Division budget will be increased by approximately 14 percent. She highlighted several NCRR funding obligations, as follows:

The Division of Biomedical Technology will initiate a new High-End Instrumentation Grant Program that will provide institutional grants to purchase commercially available instruments that cost at least $750,000. NCRR will provide support up to $2 million. The current SIG Program, which funds the purchase of instruments that cost at least $100,000, will receive approximately $49 million in FY 2002.

The FY 2002 appropriated budget also will provide $97 million to support the Research Facilities Improvement (RFI) Program, administered by the Division of Research Infrastructure. The RFI Program supports new construction of biomedical research facilities and renovations of outdated research laboratories and space. On June 7, at the meeting of the

NIH Director's Advisory Council, a Working Group of the Council will present its recommendations for awarding the additional RFI funding.

Dr. Vaitukaitis also outlined NCRR FY 2002 program plans and activities, as follows:

The Division of Biomedical Technology (DBT) will support a Biomedical Imaging Research Network that will enhance telecommunications and telemedicine activities at the NCRR-supported General Clinical Research Centers (GCRCs). DBT also will request applications for grant funding to establish Integrated Proteomic Research Centers, as presented earlier by Dr. Sheeley.

The Division of Clinical Research (DCR) will use the FY 2002 funding increase to support positions for Research Subject Advocates at GCRCs. The DCR also will work toward establishing a number of specialized laboratories and facilities at the GCRCs–neuroimaging, bioinformatics, cell sorting, genotyping, and others, as well as resources to isolate human islet cells that will be used for transplantation into Type I diabetics. DCR also will support several new clinical research training and career development programs that are underway.

The Division of Comparative Medicine (DCM) recently funded four Mutant Mouse Regional Resource Centers. These Centers are expect to quickly expand because they will be receiving mouse models created with support provided by the categorical NIH Institutes. Dr. Vaitukaitis also described a new career development opportunity for veterinary students offered by DCM. She said that half of all NIH grants include some aspect of animal research, yet veterinarians are included as the principle investigators on less than one percent of the 35,000 NIH annual awards.

The Division of Research Infrastructure (DRI) supports the Research Centers in Minority Institutions (RCMI) Program. Several centers have received American Association for Accreditation of Laboratory Animal Care (AAALAC) accreditation. In addition, research staff of several RCMIs that have clinical research centers participated in the March 2001 annual GCRC Program Directors' meeting to benefit from the vast knowledge gained by the GCRC group over the long history of the GCRC Program.

CLOSED SESSION

This portion of the NARRC 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).

NARRC 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 260 applications and recommended 259 in the total amount of $80,404,730.

ADJOURNMENT

The Council adjourned at 3:30 p.m. on May 17, 2001.

CERTIFICATION

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

/s/ June 28, 2001

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

/s/ July 3, 2001

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.