

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

**NATIONAL ADVISORY RESEARCH RESOURCES COUNCIL
MINUTES OF MEETING
JANUARY 31, 2002**

The National Advisory Research Resources Council (NARRC) convened for its 120th session at 8:30 a.m. on Thursday, January 31, 2002, in Conference Room 6, 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 2:30 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. Eon Nigel Harris
Dr. Chien Ho
Dr. Gwen A. Jacobs
Dr. Evangelia G. Kranias

Dr. William R. Morton
Dr. Judith L. Swain
Dr. James H. Wyche
Dr. Machi F. Dilworth
Liaison Member, NSF
Lt Col Alfred S. Graziano Jr., USAF
Ex-Officio, DOD
Dr. William W. King
Ex-Officio, VA

COUNCIL MEMBERS ABSENT

Dr. Roland F. Hirsch
Liaison Member, DOE
Dr. Peter O. Kohler
Dr. Michael M.E. Johns

Dr. Diana S. Natalicio
Dr. Burton A. Weisbrod
Dr. Monte Westerfield

SPECIAL INVITED GUESTS FOR OPEN SESSION

Dr. Adrian Sandra Dobs, Professor of Medicine and Oncology, Departments of Medicine, Endocrinology and Metabolism, Johns Hopkins University School of Medicine, Baltimore, Maryland
Dr. Mark Ellisman, Director, National Center for Microscopy and Imaging Research, University of California, San Diego, La Jolla, California
Dr. Ary Goldberger, Associate Professor of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts
Dr. Leslie Loew, Professor of Physiology, Director, Center for Biomedical Imaging Technology, University of Connecticut Health Center, Farmington, Connecticut

Dr. Pamela H. Mitchell, Elizabeth S. Soule Professor, Department of Biobehavioral Nursing and Health Systems, School of Nursing, University of Washington, Seattle, Washington
Dr. Stanley A. Schwartz, Professor, Department of Medicine, Division of Allergy, Immunology, and Rheumatology, State University of New York at Buffalo, Buffalo General Hospital, Buffalo, New York
Dr. Prem Srivastava, Medical Sciences Division, Office of Science, U.S. Department of Energy, Germantown, Maryland
Dr. Louis Sullivan, President, Morehouse School of Medicine, Atlanta, Georgia

STAFF OF OTHER NIH COMPONENTS

Dr. Randolph Addison, CSR/NIH
Dr. Noni Byrnes, CSR/NIH
Dr. Cheryl Corsaro, CSR/NIH
Dr. Cheryl Marks, NCI/NIH
Dr. Mary McCormick, CSR/NIH
Dr. Ramesh Nayak, CSR/NIH
Dr. Jonathan Pollock, NIDA/NIH
Dr. Karen Skinner, NIDA/NIH
Dr. Margaret Snyder, OSA/OD/NIH

OTHERS PRESENT

Ms. Victoria Contie, NCRR Research Resources Information Center, Bethesda, Maryland
Mr. Stephen Heinig, Senior Staff Associate, Division of Biomedical and Health Sciences Research, Association of American Medical Colleges, Washington, DC
Dr. Isaac Henry, Harvard Medical School, Boston, Massachusetts
Dr. Melissa Pearless, University of Pennsylvania, Philadelphia, Pennsylvania
Ms. Chris Peterson, SRI International, Menlo Park, California
Ms. Nura Shehzad, *The Blue Sheet*, Chevy Chase, Maryland
Mr. Steven Stocker, NCRR Research Resources Information Center, Bethesda, Maryland

OPEN SESSION

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

Dr. Vaitukaitis welcomed NARRC members and guests to the 120th meeting of the NARRC. She announced that the following Council members would not be present: Dr. Roland Hirsch, Dr. Michael Johns, Dr. Peter Kohler, Dr. Diana Natalicio, Dr. Burton Weisbrod, and Dr. Monte Westerfield. Five new members, recently appointed to the NARRC by Tommy Thompson, Secretary, Department of Health and Human Services (DHHS), will attend the May 2002 Council meeting. They are:

- Dr. Randall Elliott Dalton, Richmond Ear, Nose, and Throat Physicians and Surgeons, Inc. and Assistant Clinical Professor of Otolaryngology at the Medical College of Virginia;

- Dr. Mark Ellisman, Professor of Neurosciences in the Department of Neurosciences, Director of the Neurosciences Laboratory for Neurocytology, and Director of the National Center for Microscopy and Imaging Research at the University of California-San Diego;
- Dr. James Fox, Professor and Director of the Division of Comparative Medicine, and Professor in the Division of Biology, Engineering, and Environmental Health at the Massachusetts Institute of Technology;
- Dr. John Maupin, Jr., President of Meharry Medical College; and
- Dr. Paul Ramsey, Vice-President for Medical Affairs, and Dean of the School of Medicine at the University of Washington.

Dr. Vaitukaitis acknowledged the invaluable service of the following retiring Council members: Drs. Michael Johns, Chien Ho, Peter Kohler, and Evangelina Kranias.

II. Consideration of Minutes

The minutes of the NARRC meetings held on May 17, 2001, and September 13, 2001, were approved as written.

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

The next NARRC meeting will be held on Thursday and Friday, May 16 and 17, 2002. A one-day meeting is being considered. Council members will be notified of the decision.

IV. DHHS, NIH, and NCRR Personnel Update: Dr. Judith Vaitukaitis, Director, NCRR

DHHS Secretary Thompson named Donald A. Henderson, M.D. to serve as director of the newly created Office of Public Health Preparedness, which will coordinate national responses to public health emergencies, such as anthrax attacks. Dr. Henderson was the founding director of the Center of Civilian Biodefense Studies at Johns Hopkins Bloomberg School of Public Health.

Dr. Andrew von Eschenbach will become the 12th director of the NIH National Cancer Institute on February 4, 2002. Dr. Eschenbach is a nationally recognized urologic surgeon, who formerly directed the Genitourinary Cancer Center and Prostate Cancer Center Research Program at the University of Texas M.D. Anderson Cancer Center. Dr. Eschenbach replaces Dr. Richard Klausner, who stepped down as NCI director in September 2001 after serving for six years. Dr. Klausner has assumed a position as a National Academy of Sciences senior fellow and special advisor to the President for counterterrorism.

Other NIH Institute directors who have also stepped down are as follows: Dr. Enoch Gordis who directed the National Institute on Alcohol Abuse and Alcoholism, retired in December 2001 after 15 years; Dr. Stephen Hyman has left the National Institute of

Mental Health to become Provost at Harvard University; Dr. Alan Leshner left the National Institute of Drug Abuse last fall to become CEO of the American Association for the Advancement of Science (AAAS) and publisher of the AAAS journal, *Science*.

Dr. Judith Salerno, formerly with the Veterans Health Administration in Washington, DC, is the new deputy director of the National Institute on Aging.

Dr. Anthony Hayward is the new NCRRC Associate Director for Clinical Research and the Director of the Division of Clinical Research. He will oversee the following three major Clinical Research components: GCRCs, Clinical Research Resources, and Training/Career Development programs for dentists and physicians. He has been a clinical researcher for more than 20 years, supported by NIH grants. He came to NCRRC from the University of Colorado Health Sciences Center where he was professor of pediatrics, microbiology, and immunology and also served as associate director of the NCRRC-supported pediatric GCRC. Dr. Hayward is an internationally recognized investigator.

The NCRRC Office of Review has two new scientific review administrators. They are Dr. Eric Brown, who came to NCRRC from the National Heart, Lung and Blood Institute, and Dr. Mohan Viswanathan, who joined NCRRC from the Children's National Medical Center.

The NCRRC Division of Research Infrastructure (DRI) has two new staff members. Dr. Susan Kayar, a health scientist administrator, came to NCRRC from the U.S. Navy where she performed research in deep diving physiology. Dr. Sheila McClure, a health scientist administrator, came to NCRRC from Spelman College where she was an associate professor of biology and director of the Research Infrastructure in Minority Institutions (RIMI) Program.

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

Dr. Vaitukaitis referred NARRC members to a document titled "Legislative Updates" within their meeting materials, and then presented the following budget information for fiscal year (FY) 2002.

The President's budget for FY 2002 for NIH is \$23.3 billion, an increase of 14.7 percent over the FY 2001 Appropriation. The budget for NCRRC is \$1,011,594,000 in FY 2002—reflecting a 23.8 percent increase over the FY 2001 level. However, the NCRRC FY 2002 budget will be reduced to \$1,011,505,000 as a result of an across-the-board rescission of \$25 million.

The NCRRC Appropriation included \$110 million for the Research Facilities Improvement Program, \$160 million for the Institutional Development Award (IDeA) Program, and \$10 million for a new High End Instrumentation Program. The General Clinical Research Centers Program will receive an increase of approximately \$40 million, primarily to

expand clinical research career development opportunities, including K12 and K23 programs. Dr. Vaitukaitis mentioned NCRR's participation in the new NIH Loan Repayment Program for Clinical Researchers, to be addressed later in this meeting.

She discussed a number of new initiatives, some of which are underway. She concluded her presentation by describing the new Biomedical Research Infrastructure Network supported by the IDeA Program, and other new NCRR-supported resources, as follows: Human Islet Cell Resource Centers, modified operating plans for gene vector laboratories, regional resources centers for mutant mice and rats, and the Biomedical Informatics Research Network.

VI. Computational Cell Biology—Challenges and Opportunities for an Emerging Field: Dr. Leslie Loew, Director, Center for Biomedical Imaging Technology, University of Connecticut Health Center

Dr. Leslie Loew presented a report entitled *Computational Cell Biology Challenges and Opportunities for an Emerging Field*, which resulted from a roundtable discussion at the First International Symposium on Computational Cell Biology in March 2001. The report maps the future of the field and details how NCRR and NIH might participate to help this field grow.

Biology has become too complex to apply the classical scientific method without the aid of computational approaches. Computational approaches should be strongly linked to experiments so that modeling becomes a common laboratory activity, as have microscopy or chromatography. The typical applications of models developed through computational biology include: examining whether a hypothetical network is complete and correct; performing virtual knockouts before an experiment; visualizing species that can't be probed experimentally; and probing for global or emergent network properties.

The challenges in this field include managing the complexity of biological models, increasing computational intensity to provide faster simulations, handling large datasets, visualizing and interacting with models, and bridging the cultural and educational disconnects between the biological sciences and the physical and mathematical sciences.

Future opportunities that might be considered by NCRR involve developing technologies for sharing models, creating "computational cell biology centers" to provide "computationalists" within biomedical research institutions, and developing interactive electronic journals where the reader can use and modify a model online. A "grand challenge" in computational cell biology could be for NCRR to offer to the research community an opportunity to identify a multilevel, multiscale problem in cell biology that would pull together a consortium of laboratories to motivate the development of a large repertoire of computational tools and approaches.

**VII. A Report on the Research Centers in Minority Institutions (RCMI) Principal Investigators Workshop with Meetings on Future Priorities, Needs, and Directions
Dr. Louis W. Sullivan, President, Morehouse School of Medicine**

Dr. Louis W. Sullivan presented *A Report on the RCMI Principal Investigators' Workshop and Meetings on Future Priorities, Needs, and Directions*. Workshop participants deemed the RCMI Program as extremely successful in its mission of expanding and strengthening research capacities of minority health professions schools and universities. Dr. Sullivan presented information from a previous five-year period that showed a significant increase in the amount of peer-reviewed extramural funding at RCMI institutions from NIH and other sources, as well as research advances that have been published in peer-reviewed journals. Dr. Sullivan also highlighted specific accomplishments at the Morehouse School of Medicine.

On behalf of the RCMI community, Dr. Sullivan presented the following recommendations:

- (1) The profile of the RCMI Program should be elevated to congressional and public audiences in order to maintain and enhance public support for the program.
- (2) RCMI institutions should increase the number of senior investigators who can serve as research mentors for junior faculty and students.
- (3) Collaborations between RCMI institutions and among research-intensive institutions, especially medical centers, must be expanded.
- (4) Additional quantitative measures should be developed for the RCMI Program.
- (5) Animal facilities at RCMI institutions must be upgraded to meet Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), as well as other standards.
- (6) Support for research facilities and major state-of-the-art equipment maintenance and upgrades are needed to facilitate the participation in biomedical research.
- (7) A study should be undertaken to determine the potential economic and health benefits to the Nation from the elimination of health disparities.
- (8) A visiting researcher program at RCMI institutions should be developed to provide biomedical research mentors and role models.
- (9) On-site Internet2 capabilities must be provided to enable participation in national clinical trials, epidemiological studies, and studies of genetic diseases.

Dr. Sullivan said that, overall, the workshop allowed participants to share information and to learn from each other. He concluded by presenting a resolution adopted and signed by all workshop participants indicating that the NIH and the Nation are being well served by the RCMI Program and NCRR leadership.

Following his presentation, Dr. Vaitukaitis described Dr. Sullivan's many contributions to clinical research, medical education, and healthcare delivery. To honor his work, Dr. Vaitukaitis presented Dr. Sullivan a plaque "in recognition of nearly 30 years of dedication and service to the HHS, NIH, NCRR, and the RCMI community in improving

human health and welfare, and fostering excellence in biomedical research and education.”

VIII. Report on the Biomedical Informatics Research Network (BIRN): Dr. Mark Ellisman, Director, National Center for Microscopy and Imaging Research and the Center for Research on Biological Structure, University of California at San Diego

Dr. Mark Ellisman presented a *Report on the Biomedical Informatics Research Network (BIRN)*. The BIRN is an NCRR initiative aimed at creating a testbed to address biomedical researchers’ need to access and analyze various levels of aggregate data from diverse sites throughout the country. The BIRN testbed will compile hardware and develop software necessary for a scalable network of databases and computational resources. Issues of user authentication, data integrity, security, and data ownership will be addressed.

Two groups have already become BIRN partners—Mouse BIRN and Brain Morphology BIRN. The Mouse BIRN is examining animal models of disease. The initial two models allow study of demyelinating diseases such as multiple sclerosis and dopamine-related diseases such as schizophrenia. The Mouse BIRN sites consist of four institutional partnerships at the Center for In Vivo Microscopy, Duke University; Laboratory of Neuro Imaging, University of California, Los Angeles; MRI Center at Beckman Institute, part of the California Institute of Technology (CalTech), Pasadena; and the National Center for Microscopy and Imaging Research, University of California, San Diego. The Duke and CalTech sites perform MRI work; UCLA conducts multiscale histology, and UC at San Diego is engaged in 3-D microscopic imaging.

The Brain Morphology BIRN targets neuroanatomical correlates of neuropsychiatric illness. The clinical specific aims of the Brain Morphology BIRN are to determine if there are structural differences that correlate with specific symptoms such as memory dysfunction and depression. The technological specific aims are intended to further the specific clinical aims (i.e., to make it possible to quantitatively integrate information gathered across sites).

Much of the work needs to be normalized, and tools (not typically shared) need to be shared so data can be shared across the network. The Brain Morphology BIRN sites consist of the Center for Neuroimaging Technologies, Harvard University; Neuroimaging Analysis Center, Harvard University; Laboratory of Neuro Imaging, University of California, Los Angeles; the General Clinical Research Center (GCRC) at Duke University; and the GCRC at the University of California, San Diego.

XI. Scientific and Technical Review Board (STRB) on Biomedical and Behavioral Research Facilities Annual Report: Dr. Pamela Mitchell, Elizabeth S. Soule Professor, Department of Biobehavioral Nursing and Health Systems, University of Washington

Dr. Mitchell presented the FY 2000 and FY 2001 STRB Biomedical and Behavioral Research Facilities Annual Reports. For FY 2000, 90 of 94 reviewed C06 (Research Facilities Improvement Program) applications were recommended for approval at approximately \$147 million. Forty-three were funded at about \$73 million, including two from Regional Primate Research Centers and eight from centers of excellence.

In FY 2001, the STRB reviewed 81 C06 applications and 59 G20 (Animal Facilities Improvement) applications. Seventy-seven of the C06 applications were scored at a recommended level of \$133 million; NCCR funded 44, totaling \$75 million. Fifty of the G20 applications were recommended for funding at a level of about \$26 million; NCCR funded 20 grants, totaling \$12 million.

X. Complex Biological Signals: Dr. Ary Goldberger, Associate Professor of Medicine, Beth Israel Deaconess Medical Center, Harvard University

Dr. Goldberger, who heads the NCCR Research Resource for Complex Physiologic Signals, discussed the importance of open-source databases and software in carrying out new and complex advances in biomedical science, particularly those related to physiology. This new resource provides a shared repository that includes recordings of complex physiological signals, such as brain waves and heart rhythms, which enable physiologists to gain a broader understanding of disease manifestation and discover improved methods for diagnosing and treating disease.

The resource consists of three interdependent components—PhysioBank, PhysioToolkit, and PhysioNet—all of which are available online. The PhysioBank component provides access to numerous databases of well-characterized digitally recorded cardiopulmonary, neural, and other signals from both healthy subjects and patients with a variety of conditions, including cardiac arrhythmia, sleep apnea, and neurological disorders. PhysioToolKit contains a library of software for analyzing recordings, and PhysioNet provides tutorials for using the resource as well as a forum for researchers to exchange recordings and collaborate on projects.

Dr. Goldberger summarized by describing the benefits of the resource: 1) provides permanent repository for data from studies and publications; 2) establishes “gold standard” datasets; 3) protects integrity and reliability of data and analyses; 4) fosters interdisciplinary science; 5) fosters technology transfer; and 6) develops new biomarkers of disease.

XI. Categorizing Rare Disease Research as “A” Days: Dr. Anthony Hayward, Associate Director, Division of Clinical Research, NCCR

Dr. Hayward proposed a concept that potentially benefits both NCCR-supported General Clinical Research Centers (GCRCs) and patients with rare diseases. Development of therapeutics for rare diseases is unlikely to generate sufficient profits to attract industry-

supported development. The Orphan Drug Act addresses this issue and authorizes the Secretary of DHHS to make grants and/or contracts to assist in defraying the costs of qualified clinical testing of drugs, devices or foods for rare diseases and conditions. A successful partnership between the GCRCs and the Cystic Fibrosis Therapeutic Development Network (TDN) could serve as a model for a modified classification of research subjects. This modified approach will facilitate drug development for rare diseases. Dr. Hayward proposed and Council concurred unanimously that patients on drug-company-designed rare disease clinical trials may be classified by the local GCRC Advisory Committee as category A, instead of D. Investigator-initiated trials, designed by a single investigator or a consortium of investigators, not working as consultants of a commercial sponsor, are currently classified as category A. The intent of this modified approach is to enhance the development of effective therapies for patients with rare diseases.

XII. Overview of the NIH Loan Repayment Programs: Dr. Anthony Hayward, Associate Director, Division of Clinical Research, NCRR

The Loan Repayment Program (LRP) is one of several measures NIH has initiated to ensure an adequate pool of physicians and dentists who are trained to be independent clinical investigators. To be eligible for the LRP, individuals must hold peer-reviewed research funding and have educational debt that exceeds 20 percent of their salary. The NCRR Division of Clinical Research and the Division of Research Infrastructure will participate in this trans-NIH initiative but limit support to investigators who hold M.D. or D.D.S. degrees and who hold peer-reviewed funding for clinical research with human subjects.

NCRR anticipates funding at least 15 contracts in the first year and more in subsequent years. A special emphasis panel will review the investigators' personal statements of career and academic goals, descriptions of current research, research and mentoring plans, and letters of support. Those who are selected to participate in the LRP will be awarded a two-year contract under which they must conduct clinical research in consideration of the federal government agreeing to provide repayment of up to \$35,000 of an educational loan for each year of obligated service as well as tax liability reimbursements according to a pre-determined repayment schedule.

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

Dr. Ramm proposed two changes to the Council Operating Procedures. First, administrative supplemental funding increases to grants that exceed 15 percent of direct costs must be approved by the NCRR director. However, NCRR staff would continue to approve administrative supplemental funding up to 15 percent of annual direct costs.

The second proposed change to the Council Operating Procedures related to Council's expedited en bloc grant application review process via the Electronic Council Book (ECB). Dr. Ramm proposed including all scored applications (i.e. applications with

priority scores from 100 to 500) as well as all scored P41 biomedical technology center grant applications. This change parallels current NIH activities to decrease the use of paper used in the application review process by using electronic scanning and dissemination techniques instead. In this proposed NCRRC pilot process, up to 10 Council members would be selected to electronically receive summary statements through the ECB. If Council members or NCRRC staff find issues with electronically-reviewed applications, these issues would continue to be addressed in the closed session of the regularly scheduled NARRC meeting. Dr. Ramm said this new process would be tested during the next two Council review rounds. NARRC members concurred with the proposed modifications to the Council Operating Procedures.

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.

XIV. Application Review

Council considered 295 applications and recommended 294 for the total amount of \$110,501,647.

ADJOURNMENT

The Council adjourned at 3:30 p.m. on January 31, 2002.

CERTIFICATION

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

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