NIH Extramural Center Programs: Criteria for Initiation and Evaluation

Frederick J. Manning, Michael McGeary, Ronald Estabrook, Editors, Committee for Assessment of NIH Centers of Excellence Programs

ISBN: 0-309-53028-8, 230 pages, 6 x 9, (2004)

NIH EXTRAMURAL CENTER PROGRAMS

Criteria for Initiation and Evaluation

Committee for Assessment of NIH Centers
of Excellence Programs

Board on Health Sciences Policy

Frederick J. Manning, Michael McGeary, Ronald Estabrook, Editors

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS • 500 Fifth Street, N.W. • Washington, DC 20001

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

Support for this project was provided by the National Institutes of Health through Contract/Grant No. N01-OD-4-2139, TO#117. The views presented in this report are those of the Institute of Medicine Committee for Assessment of NIH Centers of Excellence Programs and are not necessarily those of the funding agencies.

Library of Congress Cataloging-in-Publication Data

NIH extramural center programs : criteria for initiation and evaluation / Committee for Assessment of NIH Centers of Excellence Programs, Board on Health Sciences Policy ; Frederick J. Manning, Michael McGeary, Ronald Estabrook, editors.
p. ; cm.
Includes bibliographical references.
ISBN 0-309-09152-7 (pbk.)
1. National Institutes of Health (U.S.) 2. Medicine—Research—Government policy—United States. 3. Medicine—Research—United States—Evaluation. 4. Medicine—Research—United States—Finance. 5. Federal aid to medical research—United States.
[DNLM: 1. Financing, Government—economics—United States. 2. Health Policy—United States. 3. Program Evaluation—United States. 4. Research Support—economics—United States. WA 540 AA1 N691 2004] I. Manning, Frederick J. II. McGeary, Michael G. H. III. Estabrook, Ronald W. IV. Institute of Medicine (U.S.). Committee for Assessment of NIH Centers of Excellence Programs.
R854.U5N535 2004
610′.72′073—dc22
2004004828

International Standard Book Number 0-309-53028-8 (PDF)

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, http://www.nap.edu.

For more information about the Institute of Medicine, visit the IOM home page at: **www.iom.edu.**

Printed in the United States of America.

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Adviser to the Nation to Improve Health

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Bruce M. Alberts is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Wm. A. Wulf is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Bruce M. Alberts and Dr. Wm. A. Wulf are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

COMMITTEE FOR ASSESSMENT OF NIH CENTERS OF EXCELLENCE PROGRAMS

RONALD ESTABROOK, (*Chair*), Professor of Biochemistry and Chair, Department of Biochemistry, University of Texas Southwestern Medical Center at Dallas

SUSAN E. COZZENS, Professor and Chair, School of Public Policy, Georgia Institute of Technology, Atlanta

IRWIN FELLER, Senior Visiting Scientist, American Association for the Advancement of Science, and Professor Emeritus of Economics, Institute for Policy Research and Evaluation, Pennsylvania State University, University Park

CHARLES K. FRANCIS, President, Charles R. Drew University of Medicine and Science, Los Angeles, California

RONALD G. GELLER, Senior Associate, Health Research Associates, Gaithersburg, Maryland

DAVID G. KAUFMAN, Professor and Vice Chair of Pathology and Laboratory Medicine, Professor of Biochemistry and of Toxicology, School of Medicine, University of North Carolina, Chapel Hill

J. RICHARD LANDIS, Director, Division of Biostatistics, Vice Chair, Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia

STEPHEN MCCONNELL, Vice President, Advocacy and Public Policy, Alzheimer's Association, Washington, D.C.

RUTH MCCORKLE, Professor and Chair, Doctoral Program, and Director of the Center for Excellence in Chronic Illness Care, Yale University School of Nursing, New Haven, Connecticut

NICOLA C. PARTRIDGE, Professor and Chair, Department of Physiology and Biophysics, Robert Wood Johnson Medical School, Piscataway, New Jersey

MICHAEL SAAG, Professor of Medicine and Director, 1917 AIDS Outpatient Clinic, University of Alabama, Birmingham

S. LEONARD SYME, Emeritus Professor of Epidemiology, Division of Public Health Biology and Epidemiology, University of California, Berkeley

MYRON L.WEISFELDT, Professor of Medicine and Director, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland

Board on Health Sciences Policy Liaison

MICHAEL LOCKSHIN, Director, Barbara Volcker Center for Women and Rheumatic Disease, and Co-Director, Mary Kirkland Center for Lupus Research, Hospital for Special Surgery, New York, New York

Study Staff

FREDERICK J. MANNING, Study Director
NATASHA DICKSON, Senior Project Assistant
BENJAMIN HAMLIN, Research Assistant

Institute of Medicine Staff

ANDREW POPE, Director, Board on Health Sciences Policy
MELVIN WORTH, Scholar-in-Residence
TROY PRINCE, Administrative Assistant, Board on Health Sciences Policy
CARLOS GABRIEL, Financial Associate

Consultant

MICHAEL MCGEARY

Independent Report Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

John S. Greenspan, University of California, San Francisco
Steven Hyman, Harvard University
David Korn, Association of American Medical Colleges
Edward D. Miller, The Johns Hopkins University
Jordan S. Pober, Yale University
David Roessner, SRI International
Joan L. Samuelson, Parkinson's Action Network
Brian L. Strom, University of Pennsylvania
Terrie Wetle, Brown University

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions

or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **William N. Kelley,** Professor of Medicine, Biochemistry, and Biophysics at the University of Pennsylvania Medical School, appointed by the Institute of Medicine, and **Floyd E. Bloom,** Chairman, Department of Neuropharmacology, The Scripps Research Institute, appointed by the NRC's Report Review Committee. They were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Preface

Research in the biomedical sciences in the United States is recognized to be at the pinnacle of success. This reputation is due in large part to the generous federal support for research provided by Congress, which appropriates the budget required to carry out the multitude of activities directed by the National Institutes of Health (NIH). This commitment by Congress over the last years is evidenced by ever increasing budgets for biomedical research. Increased funding has resulted in the ability of the scientific community to expand the portfolio of diseases studied while simultaneously developing and applying new techniques of experimentation. As a result, the biomedical sciences carried out in the United States are acknowledged to be at the forefront of major advances essential for extending the health and wellbeing of the general population.

NIH serves as the critical hub of this success. The wisdom and guidance of leaders at NIH together with the mechanisms developed over the years for selecting for support the very best ideas generated by scientists, principally in academic institutions, provide an unbeatable mix. The major share of support for research has been dedicated to funding ideas proposed by individual investigators and evaluated by a critical peer review system. However, biomedical science is changing. As our understanding of biology increases, the conduct of disease-oriented science is becoming more complex. Scientists with differing expertise and skills are now required to function as multidisciplinary teams to bring new approaches to solving complex issues. Further, the translation of basic science findings to clinical application requires unique settings where cross-disciplinary interactions and meth-

odological sharing can occur. It is this "team approach" to problem solving that one anticipates will dominate the future direction of biomedical research and thus lead to new discoveries and new therapies.

In the early 1960s the NIH established the General Clinical Research Centers program to provide loci for facilitating the cross-fertilization of scientists and clinicians that would foster the translation of fundamental science to patient care. As the years progressed the wisdom of this approach was evidenced by the establishment in the 1970s of Cancer Centers and Specialized Centers of Research for cardiovascular research. Today we note a multitude of centers that encompass a wide range of topics related to disease processes. However, support of centers is frequently expensive because of their multi-disciplinary structure and application to clinical care.

The success of centers supported by NIH has attracted the attention of members of Congress, many of whom have been urged by disease-oriented advocacy groups to seek similar funding for research in their special interests. This situation presents a dilemma for Congress and for NIH, because there is the temptation "to rob Peter to pay Paul" when dividing up the designated funding available for the support of biomedical research. Congress asked the Institute of Medicine (IOM) to carry out a study that would provide guidance to both Congress and the NIH in deciding which diseases warrant additional financial support by the establishment of new "Centers of Excellence" programs at NIH and which research areas are adequately supported by the present arrangements.

An excellent committee was established by the National Research Council and the IOM, and initial meetings revealed the large number (about 1,200) of centers that are now supported by NIH. The committee soon learned that the portfolio of centers supported by NIH is varied and the mechanisms of selection, evaluation, and initiation are not centralized at NIH. The size and funding for extramural centers supported by NIH are approximately equivalent to the size and funding of the intramural program at NIH. Likewise, the diversity of extramural centers equals the diversity of the intramural research programs supported by NIH. Much of the discussion of the committee at its five meetings was dedicated to understanding better the similarities and differences of the extramural centers supported by NIH. The committee decided at an early stage of its deliberations that a systematic approach was necessary in defining, establishing, and evaluating centers. The committee agreed that once the process of establishing new center programs is better defined and made more transparent, the joint efforts of Congress and NIH in debating the value of new center programs would be facilitated. The committee recognized the value of centers and never questioned the continued usage of this mechanism of support, in particular for translation research. Questions of the future role of centers and the shape and form into which centers will evolve in the next

decade, in particular in this period where "team research" is emphasized, remain unanswered. It is our hope that the enclosed report will continue to add to the strength and success of this multidisciplinary approach to research in the biomedical sciences.

Many individuals contributed valuable information and data to the committee through formal presentations, written submissions, or informal contacts with project staff. We are grateful to all of the following for their generous assistance: Paula Allen-Meares, James Anderson, Christine Bachrach, Kenneth Berns, Roger Bulger, Merry Bullock, Elaine Collier, Jacqueline Dunbar-Jacob, Steve Foote, Katy French, Myron Genel, John Haaga, E. Tessa Hedley-White, Kathie Hendrick, Anne Houser, Steven Hyman, Ruth Kirschstein, Steven Koslow, David Korn, Virginia Ladd, Anita Linde, Nita Maihle, Robert Moore, Creighton Phelps, Mona Rowe, John Schwab, Belinda Seto, Charles Sherman, Steven Teitelbaum, Judy Vaitukaitis, Marina Volkov, Gemma Weidlinger, Myrl Weinberg, Marion Zatz, Steven Zeisel, and Joan Levy Zlotnick.

As committee chair I am acutely aware of the contributions that the IOM staff has made to the success of the study. Special thanks and acknowledgment are due to project assistant Natasha Dickson, who made our meetings and travel as comfortable and convenient as possible, provided outstanding secretarial help throughout the study, and painstakingly copy-edited our final product. Michael Lockshin, liaison from the Board on Health Sciences Policy (BHSP), provided invaluable insight from his perspective as a former director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases. IOM Scholar-in-Residence Mel Worth and BHSP director Andy Pope provided sage advice from start to finish. I am particularly grateful to study director Rick Manning and special consultant Mike McGeary for their skilled and professional support in shepherding the committee through its task. Finally, I want to acknowledge the individual and collective contributions of the committee members. They represent an admirable example of busy but unselfish professionals volunteering their limited time tending to the scientific "commons" on which we all depend. It was a special opportunity to have worked with this outstanding group.

Ronald Estabrook, *Chair*
Committee for Assessment of NIH Centers
of Excellence Programs

Acronyms and Abbreviations

ACD	Advisory Committee to the Director
ADC	Alzheimer's Disease Center
AIDS	acquired immune deficiency syndrome
ApoE4	apolipoprotein E4
BRIN	Biomedical Research Infrastructure Network
BSA	Board of Scientific Advisers
CAM	complementary and alternative medicine
CDC	Centers for Disease Control and Prevention
CFAR	Center for AIDS Research
CJ	Congressional Justification Budget
COBRE	Centers of Biomedical Research Excellence
COSEPUP	Committee on Science, Engineering, and Public Policy
CPEA	Collaborative Programs of Excellence in Autism
CRISP	Computer Retrieval of Information on Scientific Projects
CSR	Center for Scientific Review
DBSB	Demographic and Behavioral Sciences Branch
DHHS	Department of Health and Human Services
DMD	Duchenne muscular dystrophy
DNA	deoxyribonucleic acid

EEHSR	education, epidemiology, and health services research
ERC	Engineering Research Center
EXPORT	Excellence in Partnerships for Community Outreach, Research on Disparities in Health, and Training
FDA	Food and Drug Administration
FICC	federal interagency coordinating committee
FY	fiscal year
GDP	gross domestic product
GPRA	Government Performance and Results Act
HESC	human embryonic stem cell
HIV	human immunodeficiency virus
IBD	inflammatory bowel disease
IdeA	Institutional Development Award
IMPAC	Information for Management, Planning, Analysis, and Coordination
IOM	Institute of Medicine
IRPG	Interactive Research Project Grant
MAMDC	Multipurpose Arthritis and Musculoskeletal Disease Center
MDA	Muscular Dystrophy Association
MD-CARE Act	Muscular Dystrophy Community Assistance, Research and Education Amendments of 2001
MIT	Massachusetts Institute of Technology
NCAB	National Cancer Advisory Board
NCCAM	National Center for Complementary and Alternative Medicine
NCI	National Cancer Institute
NCMHD	National Center on Minority Health and Health Disparities
NCRR	National Center for Research Resources
NEI	National Eye Institute
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases

NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NICHD	National Institute of Child Health and Human Development
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIDA	National Institute on Drug Abuse
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
NORD	National Organization for Rare Disorders
NPEBC	National Programs of Excellence in Biomedical Computing
NRC	National Research Council
NSF	National Science Foundation
OBSSR	Office of Behavioral and Social Sciences Research
OMB	Office of Management and Budget
ORD	Office of Rare Diseases
ORWH	Office of Research on Women's Health
PA	Program Announcement
PAR	PA reviewed in an institute
PAS	PA with set-aside funds
Ph.D.	Doctor of Philosophy
PHS	Public Health Service
P.L.	Public Law
R&D	research and development
RCMI	Research Centers in Minority Institutions Program
RFA	Request for Applications
RFP	Request for Proposals

RIMI	Research Infrastructure in Minority Institutions Program
RNA	ribonucleic acid
RPG	Research Project Grant
SCCOR	Specialized Center of Clinically Oriented Research
SCOR	Specialized Center of Research
SIDS	sudden infant death syndrome
SPORE	Specialized Program of Research Excellence
STAART	Studies to Advance Autism Research and Treatment
STC	Science and Technology Center
STD	sexually transmitted disease
VHA	voluntary health association

Contents

Tables, Figures, and Boxes

TABLES

FIGURES

BOXES

Executive Summary

ABSTRACT. *The National Institutes of Health (NIH) promotes advances in biomedical research primarily by supporting extramural research at colleges and universities and other nonprofit research institutions. Center awards are one mechanism of extramural support, constituting approximately 9 percent of NIH's budget. Centers are very diverse in structure and purpose, and definitions of centers and metrics for measuring their productivity are not uniformly applied across institutes, making it difficult to evaluate their effectiveness. The committee finds, however, that extramural centers offer an attractive mechanism for supporting research that benefits from a multidisciplinary, team-based approach, especially research aimed at understanding complex biomedical systems, and for translating basic scientific discoveries into useful clinical applications. The committee makes recommendations to improve the classification and tracking of center programs, clarify and improve the decision process and criteria for initiating center programs, resolve the occasional disagreements over the appropriateness of centers, and evaluate the performance of center programs more regularly and systematically. The report concludes by noting that recent changes in the nature of biomedical research, which involve opportunities to understand complex biological systems through collaborations among multiple investigators in different fields and different institutions and by assembling large-scale research infrastructures and databases, will probably result in the expanded use*

of centers and other mechanisms that support collaborative research by interdisciplinary teams.

The United States currently enjoys a remarkably productive system of biomedical research. The basis of this highly successful enterprise is the partnership of academia, government, and industry in making discoveries leading to better understanding and improved ways of preventing and treating disease and promoting health. Congress has set national biomedical research priorities and provided generous research funding. A key part of the system is the National Institutes of Health (NIH), which is the largest single source of support for biomedical research in the nation and the world.

NIH uses a variety of ways to identify and support high-quality research. The main approach is to invite investigators from throughout the country to submit their best ideas for research projects, have the proposals rated by an appropriate peer review group, and give grants for the projects considered the most promising by the peer reviewers. The research model historically has been a single investigator, working with one or two collaborators and several postdoctoral fellows, graduate students, and technicians on a specific project of three to five years duration, after which the investigator must apply for a renewal of the grant or a new award by proposing follow-up studies or a new project. These individual investigator-initiated grants are still the mainstay of NIH's extramural research program, accounting for nearly two-thirds of the research grants awarded by NIH in fiscal year (FY) 2002 and the majority of the funding for the grants.[1]

Another research model is the multi-investigator research center. In academia, centers have evolved as a structure to facilitate collaborations by multiple investigators on a research problem of common interest. NIH has supported research centers for many years as a means of encouraging interdisciplinary basic, clinical, and population-based research on scientific problems not being adequately addressed by individual investigator grants alone. Center programs are also popular with the public, organizations representing patients, and Congress, because they can bring focus, visibility, and more funding (private and public) to research on a specific disease. Every year Congress, with the encouragement of patient advocacy groups, urges

[1]In FY2002, NIH awarded 43,500 research grants, of which 63 percent were R01 (individual investigator) research project grants. R01 grants accounted for 53.4 percent of the funding ($16.8 billion). Calculated from NIH table "NIH Research Grant Awards by Fiscal Year and Activity, Fiscal Years 2000-2002"(http://grants.nih.gov/grants/award/research/rgbyact0002.htm).

NIH to establish centers for research on some particular diseases and conditions. NIH usually responds by creating a center program or by taking other initiatives it determines would be more effective in advancing research at that time. Sometimes, however, Congress directs NIH to establish centers despite NIH's view that the funding could be better spent through other mechanisms of research support. The occasion of several of these congressional mandates in recent years led to this study of the conditions in which the establishment of new center programs is appropriate. Clearly, in the view of some, congressional intervention may have a positive effect, and such input should be anticipated and integrated into the process.

A Senate amendment to the Muscular Dystrophy Community Assistance, Research and Education Amendments of 2001 specified that the "Secretary of Health and Human Services shall enter into a contract with the Institute of Medicine for the purpose of conducting a study and making recommendations on the impact of, need for, and other issues associated with Centers of Excellence at the National Institutes of Health."[2]

Although the legislation refers to "centers of excellence," the term is a general label that is not specific to a particular kind of center supported by NIH. As a result, when NIH contracted with the Institute of Medicine (IOM) in the autumn of 2002, the National Research Council established the Committee to Assess Centers of Excellence at NIH and charged it to:

> …conduct a one-year study of the use of research centers at the National Institutes of Health. The study will focus on the criteria and procedures used in deciding to adopt the use of centers, how they are designed and administered, comparisons with other mechanisms of research support, their impacts and costs, and how they are evaluated as a mechanism (as well as how individual centers are evaluated). The emphasis will be on how NIH uses centers as a program mechanism, compared with other mechanisms, rather than on how individual centers are chosen for awards. The committee will prepare a consensus report with findings and recommendations for improving the use of the center mechanism, given the many factors that must be taken into account in a specific area of research, including the state of the science, presence of promising research opportunities, burden of disease, need for interdisciplinary approaches, alternative mechanisms (e.g., research project grants, program project grants, and contracts), and adequacy of the research infrastructure. The report will include recommended criteria and processes for deciding whether research centers should be created.

[2]P.L. 107-84, Muscular Dystrophy Community Assistance, Research and Education Amendments of 2001, Sec. 7, Study on the Use of Centers of Excellence at the National Institutes of Health.

CURRENT USE OF CENTER AWARDS

Center grants and cooperative agreements (hereafter called grants) have constituted between 8 percent and 9 percent of the total NIH budget each year for more than a decade. In February 2003 NIH reported that it planned to fund 1,209 extramural research center grants at an annual cost of $2.4 billion in FY2003. Investigators in every state won center grants in FY2002. Every NIH institute funds center grants, with FY2001 totals ranging from 13 center awards (National Institute of Dental and Craniofacial Research) to more than 300 (National Center for Research Resources). The median number of awards funded by an institute was 33. Grants for specialized centers were most numerous in FY2001, totaling 383. The next most numerous were the 318 awards for "core" grants that fund center infrastructure but no actual research. Specialized centers were the most expensive, with grants averaging $2.2 million in FY2001 (not counting General Clinical Research Centers, also averaging $2.2 million, and Primate Centers, averaging $7.5 million).

Close analysis of NIH Requests for Applications (RFAs) and Program Announcements (PAs) led the committee to conclude that these data, though generally useful, have some shortcomings. Specifically, not all centers are funded by center awards and some programs without the word "center" in their names are center programs in terms of goals, structure, and activities. The committee suggests a set of definitions for three types of center awards:

- *Center Infrastructure* awards or "core" grants support administrative and technical services required by a group of investigators whose research is funded by independently obtained research grants. The primary goal is to focus research on a particular set of questions and increase efficiency.
- *Research Center* awards fund not only common services but research projects as well. In some cases, they may also support additional activities such as community education, screening and counseling programs, and educating medical and allied health professionals about state-of-the-art diagnostic, prevention, and treatment techniques.
- *Research Resource Center* awards develop and provide specialized research resources, services, and tools to researchers across the country. Examples of their products include animal models, microarrays for genomic analyses, and islet cells for transplantation in patients with diabetes.

The committee sees a need for NIH to adopt this set of definitions or develop a similar classification scheme and then consistently identify all activities meeting one of those definitions as centers, regardless of the name of the program or the current funding mechanism. The committee also

noted that the large category of research resource centers, those with the primary mission of developing and supplying scientists with research tools and resources such as specially bred animals, are not central to the congressional concerns that led to the current study and are therefore not included in subsequent discussion of centers in this report.

Finding. NIH does not consistently apply either the term center or the budget mechanism category for center awards to extramural research centers. This inconsistency makes it difficult to describe accurately the extent of research funding devoted to support of centers or evaluate the relative effectiveness of center awards or how well center programs complement other NIH-funded activities.

Recommendation 1. NIH should adopt or develop a coherent classification system with functional criteria that should be uniformly applied across all institutes for the categorization of all NIH centers. The three functional categories of centers offered above by the committee represent one possible system of classification. All activities that fit in one of the categories in the classification system adopted or developed by NIH should be identified as centers, regardless of the name of the program or mechanism of funding.

INITIATION AND MANAGEMENT OF CENTER PROGRAMS

The impetus for NIH support of research centers comes from many sources. Centers established since the beginning of 2002 have been suggested by external advisory groups, NIH institute strategic plans, scientific workshops supported by NIH, NIH program staff, a federal interagency coordinating group, advocacy organizations, Congress, a national commission, and an IOM report.

New initiatives, such as center programs, are considered for adoption in NIH's annual planning and budgeting process. That process is elaborate and open, involving input from external advisory groups, meetings with voluntary health associations and patient advocacy groups, and review by an institute's national advisory council. It is a very decentralized process that varies from institute to institute, but it is generally informal in terms of procedures and criteria for adopting new programs. The process for deciding on the design and management of a new program initiative is also decentralized to the institutes, including the requirements and criteria for reviewing applications for center funding and the choice of the award to be used to support the centers that are approved for funding.

The current criteria for center programs can be gleaned from the discussion of program purposes and descriptions of center activities and com-

ponents in recent PAs and RFAs for center programs, which include the following rationales:

1. The scientific opportunities and/or health problems that the center program would address have high priority at the institute.
2. Centers would facilitate activities that are most effectively undertaken by teams of investigators working in close proximity, such as:

- multidisciplinary collaborations for problems that require diverse scientific backgrounds;
- multi-investigator teams capable of a wide scope of research activities;
- translating the results of basic research into clinical practice;
- supporting existing and stimulating new investigator-initiated applications for research program grants;
- training graduate students, postdoctoral fellows, and other health professionals in cross-disciplinary or translational research;
- attracting experienced researchers into a new area of research;
- networking with other centers in the program to conduct coordinated research activities beyond the capacity of any single center, for example, by recruiting larger numbers of patients into common research protocols.

3. The centers program would provide critical research resources that are difficult or too expensive to develop in most individual laboratories.
4. The centers would build infrastructure to promote institutional development of a field of research (e.g., nursing, population research), state-of-the-art biomedical and behavioral research at minority-serving institutions or institutions in regions with little NIH research funding, and community education and outreach programs.

The committee makes several recommendations aimed at making the process for assessing the appropriateness of research centers more explicit and consistent, developing and applying a uniform set of key questions to ask in deciding to establish a new center program (a list of such questions is suggested), and providing a mechanism to adjudicate disagreements over the need for centers as they arise.

Finding. Proposals to establish center programs originate from many sources within and outside NIH, including scientific workshops, internal program reviews, national advisory councils and other advisory bodies, NIH professional staff, professional scientific societies, citizen groups, the

executive branch, and Congress. Although each of the institutes has a planning process for setting priorities and developing programs, the procedures and criteria for assessing the appropriateness of centers in an area of research are not explicit or uniform. The national advisory councils are currently required to review all initiatives, but given the small amount of time they can devote to the task, effective arrangements for soliciting external advice in the approval process and clear and consistent criteria for program approval (see next recommendation) are critical elements of center program initiation.

Recommendation 2. NIH should make explicit its process for deciding whether establishment of a new center program is appropriate to meet a specified goal. The key elements of the process, which should be consistent across institutes, necessarily involve broad input from the extramural scientific community and incorporation of the views of the public. NIH needs to inform Congress and advocacy groups of the process and of the opportunities they will have to provide input.

Finding. The rationale for initiating a center program stated in concept papers or in the PAs and RFAs does not always indicate why a program of centers is a better means for achieving program goals than other mechanisms of research support. The scientific rationale for adding centers to the mix of funding mechanisms in a specific area is not usually made explicit, and the comparative advantage of using centers to accelerate progress is not always shown.

Recommendation 3. A uniform set of key questions to ask in establishing each program of centers, such as those listed in Box ES-1, below, should be developed and adopted by NIH. The recommendation to establish any program of centers should be supported by positive responses to the relevant questions on the list that NIH adopts.

Finding. NIH is occasionally urged to establish centers by Congress or by groups advocating greater federal action on a specific disease or other health issue about which NIH scientists believe the knowledge base or the number of active researchers, or both, are too small to support an effective center program. Even if the process and criteria for reaching this conclusion are made more open and explicit, and involve broad input from the scientific and advocacy communities (see Recommendation 2), differences among stakeholders and scientific experts may still exist. Congressional hearings may not provide the optimal forum for resolving these differences. A need exists for an advisory mechanism to assist Congress and NIH when there is continuing disagreement about the need for centers for a specific disease or other health issue.

BOX ES-1
Suggested Criteria for Initiation of Center Programs

	Center program may be the right mechanism if…	Another mechanism is more appropriate if…
Both Center Infrastructure (Core-Type) and Research Center Programs Should Meet the Following Criteria.		
Importance of the problem: Is the area of research important enough to warrant a concentration of resources?	The area of research has been declared a high priority by the institute in its planning process.	The area of research is a lower priority for the institute.
Need for core resources: Do shared resources in this area provide economies of scale?	The area of research relies heavily on specialized resources not provided in normal university services but difficult to include in research project or program project (i.e., R01 or P01) budgets.	The area of research can proceed with standard university services, or individual investigators can access the services cost-effectively.
Center Infrastructure (Core-Type) Programs Should Meet the Following Additional Criteria.		
Concentrations of projects: Do enough investigators at one university or in close proximity already have funded projects in this area?	The proposed program or award can justify in detail that there are enough users for the shared services.	The number of documented potential users is well below the capacity of the proposed shared resources.
Research Center Programs Should Meet the Following Additional Criteria.		
Sufficient number of investigators: Are there enough people working in the field to support the level of effort proposed?	There are, or potentially are, plenty of strong investigators in the area, so that there will be real competition for the center awards.	There are few investigators, or little potential for more investigators working in development with noncenter grants.

Need for strategic focus: Does this research area need some coordination among projects to build toward or accelerate important findings?	Scattered findings from a number of research groups are leaving critical gaps in the knowledge base. These groups need to articulate a larger-scale, more coordinated research program to make or accelerate progress.	Individual grants or P01s are already moving the field forward rapidly based on shared understanding of the critical methods and problems.
Need for interdisciplinary interaction: Would the research problem benefit from an interdisciplinary approach that is not happening now?	Current grant-supported research is largely single-discipline, and credible, independent advisors recommend an interdisciplinary approach.	Current R01 and P01 research is already interdisciplinary.
Need to identify research problems with translational potential: Does the clinical community perceive that their problems are not being addressed?	The clinical or other practice community can provide a significant body of questions that research could address to help them solve problems but is not currently producing. The list of questions should be articulated, and the match against existing knowledge should be documented with a literature search.	The clinical or other practice community is already absorbing a high level of research knowledge and has significant influence on the research agenda of basic research related to the problem.
Need to stimulate translational activities: Does the basic science community perceive that their findings are not being taken up?	There is a large body of knowledge that is not being translated into clinical or public health practice. The program should be able to quantify the size of that body of knowledge with publications.	Basic research related to the problem is already being fully utilized in clinical research, drug development, clinical practice, or public health.
Need to provide distinctive training environments	Researchers trained in existing modes in the field are being prepared too narrowly to meet the challenges of problem-solving in this area, or are missing critical skills.	Existing training is giving Ph.D.s and physicians the key skills and knowledge they need for their career paths.

Recommendation 4. In those occasional instances in which disagreement continues over the need to establish a new center program, the NIH director or congressional committee chairman should request that an advisory committee be appointed by the Secretary of Health and Human Services to review the evidence in support of a developing initiative for a centers program and assess whether the proposed program meets the prestated criteria for the establishment of centers.

EVALUATION OF CENTER PROGRAMS

NIH, like other federal research agencies, takes several approaches to evaluating the performance of its programs. One is technical review by a panel of external experts knowledgeable in the area of research involved and perhaps users of the research results. Another approach is formal evaluation based on data collected by external contractors.

As described in Chapter 3, a proposal to establish a program of research centers in the first place undergoes a prospective review process, which varies from institute to institute but generally involves an external committee or workshop to obtain input on the goals and design of the proposed centers, as well as the required review and approval by a chartered external advisory body (usually the institute's national advisory council) and clearance of the RFA or PA inviting applications for center support through the Office of Extramural Programs in the Office of the Director of NIH.

Research programs may also undergo retrospective evaluation. Each ongoing as well as proposed center program must justify itself in the annual planning and budgeting process. In addition, some of the institutes engage in a formal "visiting committee" process, that is, an external panel of experts, usually a subcommittee of the institute's national advisory committee for a major program division that reviews the division's programs on a regular schedule. This process can lead to changes in center programs or proposals to initiate new center programs.

From time to time, institute staff members, the institute director, or the national advisory council decides that a center program should be reviewed by staff, an external committee of experts, or a combination of staff and outside experts for its continuing effectiveness and/or relevance. Examples of reports from such ad hoc exercises are summarized in Appendix F. Generally the reports are based on the experience and expert judgment of committee members, because for reasons discussed below, objective measurement and analysis of a program's performance, especially in terms of outcomes and impact, are difficult to obtain and frequently require resources and technical skills beyond that provided to the committees.

Finding. NIH does not have formal regular procedures or criteria for evaluating center programs. From time to time, institutes conduct internal program reviews or appoint external review panels, but usually these ad hoc responses are done in response to a perception that the program is no longer effective or appropriate rather than as part of a regular evaluation process. Most of these reviews relied on judgment by experts rather than systematically collected objective data, although some formal program evaluations have been performed by outside firms using such data.

Recommendation 5. Every center program should be given a formal external retrospective review for its continued effectiveness on a regular basis (at least every five to seven years). The review should be coordinated at an organizational level above the centers program itself.

a) The review should be performed by people at arms-length distance from the program and with the appropriate expertise to judge the varied activities of the centers. The views of interested publics, including the scientific and advocacy communities, as well as NIH officials and grantees, should be solicited as a matter of course.

b) The program should be evaluated against its original objectives and with regard to the changed circumstances of its field. The review should include consideration of the question, "Are centers still the most appropriate means of making progress in this field?" and the criteria should be consistent with those adopted or developed in response to Recommendation 3 for establishing the center program in the first place.

c) The review should use multiple sources of evidence to evaluate the effectiveness of the program, and its conclusions should be evidence-based. The review might consider, for example, the scientific impact (e.g., publication counts and impacts, important discoveries, development and sharing of research tools); impact on human health (e.g., changes in health status); and impact on human resources (e.g., career paths of pre- and postdoctoral students and investigators).

d) A program evaluation plan should be developed as part of the design and implementation of new center programs, and data on indicators used in the evaluation plan should be collected regularly and systematically. Data collected from the centers should conform to a common format. Many of the indicators should also be useful for program monitoring and progress reporting. One set of potential indicators is provided in Box ES-2.

e) Each institute's plan for evaluating center programs should be linked to its strategic planning process.

BOX ES-2
Potential Indicators for Evaluating NIH Center Programs

Goal:	Increased basic and clinical research in program's area of focus.
Indicators:	Increased number of studies in each category being funded, especially new studies; increased number and impact of publications and presentations of center research.
Goal:	More multidisciplinary research.
Indicators:	Increased number of collaborations established; increased number and percent of center studies, especially center scientific publications authored by teams of scientists from two or more university departments; greater number of disciplines represented among center-affiliated staff.
Goal:	More translational research.
Indicators:	Increased number of publications in clinically oriented journals; patent applications; licenses issued; and clinical trials under way or completed.
Goal:	Increased or more effective support, or both, for independently funded investigators.
Indicators:	Larger number of studies supported, especially new studies; more types and amounts of support supplied; characteristics of core facilities, materials, and services available; increased number of publications of center-affiliated investigators.
Goal:	Increased attention to program's area of focus by centers' home institutions, scientific community, and general public.
Indicators:	Increased institutional support for center operations (space, faculty and staff, recognition on institutional organizational charts and publications); additional research funding from NIH and other public agencies, nonprofit organizations, and commercial industry.

CONCLUDING COMMENTS

Center programs are a small but important element in NIH's array of tools to address its dual mission of pursuing fundamental knowledge about the nature and behavior of living systems and of bridging the gap between basic science discoveries and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.

Judging from the pronouncements of a number of leaders in the field, including the present director of NIH, support for centers and similar mechanisms might well grow significantly over the next decade. Elias Zerhouni, the NIH director, recently summarized the results of a series of

Goal:	Successful recruitment of established researchers to the program's area of interest.
Indicators:	More scientists with previous publications in the area joining the center; increased number of new grants or other funding obtained by these new investigators; number of publications, patents, or other products of work at the centers.
Goal:	Development of new investigators.
Indicators:	More trainees associated with the programs' centers; current positions of former trainees; research grants subsequently won by these trainees at program centers or elsewhere; larger number of trainees who are elected members or fellows of professional societies.
Goal:	Expanded education of health professionals.
Indicators:	Increased number of courses, seminars, and workshops offered by program centers; larger number of health professionals attending.
Goal:	Expanded education of the general public.
Indicators:	Increased number of publications in the popular press, radio or television appearances by center staffs, increases in patient load for relevant health problems; increased percentage of patients agreeing to participate in clinical research.
Goal:	Demonstration of state-of-the-art prevention, diagnosis, and treatment techniques.
Indicators:	Increased number of seminars, grand rounds, workshops, and other educational programs conducted; larger number of local and regional practitioners participating in such programs.

meetings he convened to develop a Roadmap for Medical Research, defined as a short list of initiatives that would make the biggest impact on biomedical research.[3] The meetings, which included leading extramural scientists

[3]On September 30, 2003, after this report was drafted, NIH made public the initiatives it is planning to implement the "Roadmap for Medical Research" (Zerhouni, 2003). As expected, new center programs will play a prominent role in implementing the Roadmap objectives. In September and October 2003, NIH issued eight RFAs under the Roadmap, five of them for new center programs. They include: National Centers for Biomedical Computing (U54); National Technology Centers for Networks and Pathways (U54); Exploratory Centers for Inter-

as well as NIH institute directors, resulted in three major themes, at least two of which have been driving forces behind the establishment of center programs in the past, the need for more multidisciplinary team-based research and the need to reengineer the national clinical enterprise for faster translation of scientific discoveries into clinical reality. Although certain obstacles to collaborative research discussed in the last chapter must be overcome, this committee expects to see center programs continue and expand, because they are well suited for addressing certain kinds of research priorities, especially turning important scientific discoveries into clinically useful applications.

REFERENCES

Kaiser, J. 2003. Speeding up Delivery: NIH aims top push for clinical results [News]. SCIENCE 2003 (5642):28-29.

Zerhouni E. 2003. Opening Statement on the FY2004 President's Budget Request, "FY 2004 Appropriations Overview," Hearing before the House Appropriations Subcommittee on Labor, Health and Human Services, and Education, April 2, 2003. [Online]. Available: http://www.nih.gov/about/director/budgetrequest/FY2004budgetrequest.htm [accessed May 20, 2003].

disciplinary Research (P20); Development of High Resolution Probes for Cellular Imaging (P20); and Centers for Innovation in Membrane Protein Production (P50). At least three more center programs are planned: Nanomedicine Centers, Bioactive Small Molecule Library and Screening Centers, and Regional Translational Research Centers. Funding over six years is planned to be $2.1 billion, or $350 million a year on average, although funding in the first year (FY2004) will be approximately $128 million (Kaiser, 2003). According to the five center program RFAs, up to $45 million has been set aside for center awards in FY2004.

1

Introduction

The United States currently enjoys a remarkably productive system of biomedical research. The basis of this highly successful enterprise is the partnership of academia, government, and industry in making discoveries leading to better understanding and improved ways of preventing and treating disease and promoting health. Congress has set national biomedical research priorities and provided generous research funding. A key part of the system is the National Institutes of Health (NIH), the largest single source of support for biomedical research in the nation and the world. Industry also invests heavily in biomedical research, but NIH provides the bulk of the support for basic and clinical research that is still far from commercial payoff but is essential for the development of new treatments several years in the future. To take advantage of the rich talent of American scientists, NIH carries out its mission of advancing science and its applications primarily by supporting extramural research, that is, research conducted by investigators in universities, academic health centers, and independent research institutes. In addition to producing extraordinary scientific and medical advances, the policy of supporting research in academia insures a continuing supply of well-trained researchers, because graduate students and postdoctoral fellows are able to learn by participating in cutting-edge research.

NIH uses a variety of ways to identify and support high-quality research. The main approach is to invite extramural investigators to submit their best ideas for research projects, have the proposals reviewed and rated by an appropriate peer review group, and give grants for the projects con-

sidered the most promising by the peer reviewers. The research model historically has been a single investigator working with one or two collaborators and several postdoctoral fellows, graduate students, and technicians on a specific project of three to five years duration, after which the investigator must apply for a renewal of the grant or a new award by proposing follow-up studies or a new project. These individual investigator-initiated grants are the mainstay of NIH's extramural research program, accounting for nearly two-thirds of the research grants awarded by NIH in fiscal year (FY) 2002 and the majority of the funding for the grants.[1] Another research model is the multi-investigator research center. In academia, centers have evolved as a structure to facilitate collaborations by multiple investigators on a research problem of common interest. NIH has supported research centers for many years as a means of encouraging interdisciplinary basic, clinical, and population-based research on scientific problems not being adequately addressed by individual investigator grants alone. Over the past decade NIH support for such grants has consistently constituted between 8 and 9 percent of the total NIH budget.[2]

Box 1-1 provides NIH's definition of a research center grant. As the definition suggests, center grants are used in a variety of circumstances for a variety of purposes. Chapter 2 explores this variety in more detail, but the committee believes that it is useful to conceive of center grants as members of one of three general types:

1. *Center Infrastructure* awards, or "core" grants, support administrative and technical services required by a group of investigators whose research is funded by independently obtained research grants. The primary goal is to focus research on a particular set of questions and increase efficiency.
2. *Research Center* awards fund not only common services but research projects as well. In some cases, they may also support additional activities such as community education, screening and counseling programs, and educating medical and allied health professionals about state-of-the-art diagnostic, prevention, and treatment techniques.

---

[1]In FY2002, NIH awarded 43,500 research grants, of which 63 percent were R01 (individual investigator) research project grants. R01 grants accounted for 53.4 percent of the grant funding ($16.8 billion). Calculated from NIH table "NIH Research Grant Awards by Fiscal Year and Activity, Fiscal Years 2000-2002" (http://grants.nih.gov/grants/award/research/rgbyact0002.htm).

[2]NIH also employs a number of types of research grants other than those for centers and individual-investigator research projects, including research project grants for multi-investigator research, cooperative agreements for clinical trials, and research career awards. NIH also gives research training awards, issues research and development contracts, and supports an intramural research program (see section, Background on NIH, below).

BOX 1-1
NIH Research Center Grants

Research Center grants are awarded to extramural research institutions to provide support for long-term multidisciplinary programs of medical research. They also support the development of research resources, aim to integrate basic research with applied research and transfer activities, and promote research in areas of clinical applications with an emphasis on intervention, including prototype development and refinement of products, techniques, processes, methods, and practices.

SOURCE: *National Institutes of Health FY2001 Investments. April 2001.* (http://www.nih.gov/News/BudgetFY2002/FY2001investments.htm#centers).

3. *Research Resource Centers* develop and provide specialized resources, services, and tools to researchers across the country. Examples of their products include animal models, microarrays for genomic analyses, and production of islet cells for transplantation in patients with diabetes.

The first two types of center programs are especially popular with the public, organizations representing patients, and Congress, because they can bring focus, visibility, and, often, more funding (private and public) to research on a specific disease. A citizen with cancer, for example, is more likely to be aware of the existence of a nearby NIH-funded cancer center than to know that the National Cancer Institute (NCI) is also supporting more than 6,000 individual research projects across the country.

Centers for research on AIDS, Alzheimer's disease, Parkinson's disease, and many other diseases and conditions play a similar role. Establishing research centers is also seen as an effective and at times necessary way to expedite the translation of basic research advances into clinical practice—for example, better diagnoses and treatments—while providing state-of-the-art care to patients participating in the research.

Every year Congress, with the encouragement of patient advocacy groups, urges NIH to establish various new centers for particular diseases and conditions. Usually NIH responds by creating a center program or by taking other initiatives it determines would be more effective in advancing research at that time. Sometimes, however, Congress directs NIH to establish a new center program despite NIH's view that centers would not be the most effective approach to the research/disease problem being addressed and therefore that funding directed towards establishment and support of the center would be better spent differently. The occasion of several of these congressional mandates in recent years led to this study of the conditions in

which the establishment of center programs is appropriate. Clearly, in the view of some, congressional intervention may have a positive effect, and such input should be anticipated and integrated into the process.

There is certainly evidence that center programs can be and have been very productive ways to organize research. For example, collaborative research among Alzheimer's Disease Centers supported by the National Institute on Aging has led to a number of discoveries, including the finding that one form of apolipoprotein E is an inherited risk factor for the development of sporadic Alzheimer's disease and that familial Alzheimer's disease is linked to genes on chromosomes 21, 14, and 1 (NIA, 2001). There are a number of other examples of multicenter collaborations among ADCs in which pooling clinical and pathological information from a large number of patients and controls has helped advance understanding of the pathological basis of dementia. These include development of the Alzheimer's Disease Assessment Scale, Clinical Dementia Rating Scale, and criteria for neuropathological diagnosis of Alzheimer's disease and identification of Mild Cognitive Impairment as a precursor of dementia.

Among the other contributions of centers are those of the Centers for AIDS Research (CFARs) supported by the National Institute of Allergy and Infectious Diseases (NIAID) and other institutes. One example is a collaboration of two CFARs on a bench-to-bedside or translational research project which showed that a peptide designed and synthesized to interfere with the replication of HIV worked in an animal model. Next, the centers demonstrated proof of concept in humans in a Phase I clinical trial (OAR, 1999). The peptide (T-20, or enfuvirtide) was then developed by industry, approved by the Food and Drug Administration (FDA) in the spring of 2003, and is now the cornerstone of salvage therapy for HIV-infected patients in the developed world. The use of plasma HIV RNA (viral load) was developed at a CFAR that had established a specimen repository and hosted basic research projects supported by R01 individual-investigator grants. The first description of viral dynamics of HIV was made at two CFARs working on drug development with several pharmaceutical companies and in which basic research by R01-supported investigators helped lead to the findings.

A long-term study conducted in Comprehensive Sickle Cell Centers supported by the National Heart, Lung, and Blood Institute (NHLBI) recently showed that the drug hydroxyurea prolongs the life of sickle cell anemia patients with moderate to severe forms of the disease (a 1995 study had shown that hydroxyurea reduced symptoms and the need for hospitalizations and transfusions by half among such patients and led to its approval by the FDA as the first drug for treatment of sickle cell disease) (Steinberg et al., 2003). A clinical trial at a specialized center of research on osteoporosis supported by the National Institute of Arthritis and Muscu-

loskeletal and Skin Diseases (NIAMS) was one of two recent studies showing that combining two effective treatments for osteoporosis does not improve bone mineral density more than using either treatment alone, a finding that should reduce medical costs by discouraging the use of the more expensive combination therapy (Finkelstein et al., 2003).

Despite successes like these, establishing research centers may not always be the best research strategy. To be cost effective, the advantages of research centers must outweigh the initial investment in infrastructure, extra costs of managing the program, additional costs of center administration, and reduced flexibility in the institute's budget imposed by a relatively large and long-term funding commitment. As a brief introduction to an analysis developed in detail in Chapter 4 of this report, a minimum set of criteria for initiating a center program should include the existence of promising research opportunities that are uniquely suited to the center approach or can be pursued better or faster through center support than individual project grants, enough qualified and interested investigators to form the nucleus of leadership for the centers, and a reasonable expectation that institute's budget can support a long-term commitment to the center program without compromising the institute's balanced research portfolio. Chapters 3 and 4 address the process and criteria that would help guide NIH and the Congress, as well as inform advocacy and other interested parties, about the circumstances in which a program of centers would be the most appropriate mechanism of research support.

There is also good reason to believe that demand for centers and other organizational forms for conducting coordinated and collaborative research programs by interdisciplinary teams will increase in the future. This demand is arising from two related trends: the growth of large-scale biomedical science typified by the sequencing of the human genome (IOM and NRC, 2003) and the increasing opportunities for translating advances in the understanding of biological systems into better ways of preventing, screening, diagnosing, and treating diseases (Zerhouni, 2003a). For example, the National Institute of General Medical Sciences (NIGMS), which emphasizes basic research and historically has relied on individual investigator grants, has recently begun a number of new initiatives for better basic understanding of complex biological systems that involve the creation of center programs and other organizational arrangements—such as consortia, alliances, and networks—for creating large interdisciplinary and interinstitutional teams and establishing an infrastructure for integrating results through systematic analysis. These initiatives stem from a planning exercise during 1997 and 1998 in which advisory groups expressed the view that, in addition to continuing its long-time support of research elucidating the individual steps in biological processes at the subcellular and molecular level, it was time for NIGMS to begin to develop mechanisms to gain a

basic understanding of entire integrated biological systems, a complex effort that would require an integrated effort by many kinds of scientists (NIGMS, 1998). Other institutes have been receiving similar advice and establishing similar initiatives.[3]

The need for teams to pursue cutting-edge science in systems biology is also a major theme in the NIH Roadmap for Medical Research, a strategic planning exercise conducted by Dr. Elias Zerhouni, the new director of NIH, in the summer of 2002. One of the major conclusions of the exercise was, "Because of the complexity and scope of today's scientific problems, traditional 'mentor-apprentice' models must be replaced by integrated teams of specialists from numerous disciplines that were considered unrelated in the past" (Zerhouni, 2003a).[4] Accordingly, "To foster the creation of multidisciplinary teams of experts in biology, behavior, engineering, mathematics, chemistry, physics, informatics, and clinical research, the NIH will initiate new programs that emphasize support for groups of investigators with diverse expertise who are able to bring forth proposals with novel prospects for scientific advances" (NIH, 2003).[5]

Research universities are also responding to changes in the nature of scientific investigation by creating large interdisciplinary research and educational centers. For example, the Massachusetts Institute of Technology, Harvard University, and the Whitehead Institute for Biomedical Research are establishing a joint research institute as a vehicle for bringing together experts in biology, medicine, chemistry, engineering, and computer science in large-scale projects to determine the molecular causes of disease by sys-

[3]See, for example, the minutes and consensus report of a special emphasis panel on integrative research formed by the NHLBI in 1996 (NHLBI, 1996).

[4]In addition to "Changing dynamics of the research teams of the future," other major themes of the Roadmap were: "New pathways to scientific discovery" (including integrative interdisciplinary research focused on understanding how complex biological systems operate) and "Need to re-engineer the national clinical research enterprise for optimal translation of our discoveries into clinical reality."

[5]On September 30, 2003, after this report was drafted, NIH released the first initiatives of the Roadmap. New center programs were a major feature of this effort "to remove some of the biggest roadblocks that are keeping research findings from reaching the public as swiftly as possible" (Zerhouni, 2003b). Requests for Applications (RFAs) have been issued for five new center programs (National Technology Centers for Networks and Pathways, National Centers for Biomedical Computing, Exploratory Centers for Interdisciplinary Research, Development of High Resolution Probes for Cellular Imaging, and Centers for Innovation in Membrane Protein Production) and at least three more center programs are in the planning stage (Nanomedicine Centers, Bioactive Small Molecule Library and Screening Centers, and Regional Translational Research Centers).

tematically examining genes and proteins. The institute is seen by its sponsors as a "new model" intended to "complement existing research efforts by serving as a catalyst and nucleus for larger collaborative projects that cannot readily be accomplished in the traditional setting of individual academic laboratories—for reasons such as a need for scale, scientific or organizational infrastructure, or multidisciplinary expertise." Accordingly, the institute will include "both individual research laboratories and larger, team-based programs to produce and employ genomic tools" (MIT, 2003). Similar initiatives include the Institute for Integrative Genomics at Princeton University, Bio-X Program for Bioengineering, Biomedicine and Biosciences at Stanford University, Interdisciplinary Research Institute at the University of Chicago, and Health Sciences Initiative at the University of California at Berkeley.

CHARGE TO THE COMMITTEE

A Senate amendment to the Muscular Dystrophy Community Assistance, Research and Education Amendments of 2001[6] specified that the "Secretary of Health and Human Services shall enter into a contract with the Institute of Medicine for the purpose of conducting a study and making recommendations on the impact of, need for, and other issues associated with Centers of Excellence at the National Institutes of Health."

Specifically, the legislation called for the Institute of Medicine (IOM) to consider:

> (1) The current areas of research incorporating Centers of Excellence (which shall include a description of such areas) and the relationship of this form of funding mechanism to other forms of funding for research grants, including investigator-initiated research, contracts, and other types of research support awards.
>
> (2) The distinctive aspects of Centers of Excellence, including the additional knowledge that may be expected to be gained through Centers of Excellence as compared to other forms of grant or contract mechanisms.
>
> (3) The costs associated with establishing and maintaining Centers of Excellence, and the record of scholarship and training resulting from such Centers. The research and training contributions of Centers should

[6]P.L. 107-84, Muscular Dystrophy Community Assistance, Research, and Education Amendments of 2001, Sec. 7, Study on the Use of Centers of Excellence at the National Institutes of Health.

be assessed on their own merits and in comparison with other forms of research support.

(4) Specific areas of research in which Centers of Excellence may be useful, needed, or underused, as well as areas of research in which Centers of Excellence may not be helpful.

(5) Criteria that may be applied in determining when Centers of Excellence are an appropriate and cost-effective research investment and conditions that should be present in order to consider the establishment of Centers of Excellence.

(6) Alternative research models that may accomplish results similar to or greater than Centers of Excellence.

Although the legislation refers to "centers of excellence," the term is a general label that is not specific to a particular kind of center supported by NIH. Not all legislatively mandated centers are centers of excellence, and NIH has initiated centers of excellence programs in the absence of congressional or advocacy group interest. NIH also supports several programs that fund entities that function like centers (and use center grants) but are called "programs of excellence." NIH does not always use the title "centers of excellence," even though the legislation establishing a center program does. Finally, several programs called centers of excellence that are of interest to advocacy groups and Congress are not supported with center grants. IOM staff thus sought guidance about the scope intended, and Senate staff confirmed that the study was meant to include all NIH-supported research centers, whether or not they are formally called centers of excellence.

In September 2002 the NIH Office of Extramural Research contracted with IOM to conduct the study, and at the request of IOM, the National Research Council established the Committee for Assessment of NIH Centers of Excellence Programs. The committee was charged to:

> … conduct a one-year study of the use of research centers at the National Institutes of Health. The study will focus on the criteria and procedures used in deciding to adopt the use of centers, how they are designed and administered, comparisons with other mechanisms of research support, their impacts and costs, and how they are evaluated as a mechanism (as well as how individual centers are evaluated). The emphasis will be on how NIH uses centers as a program mechanism, compared with other mechanisms, rather than on how individual centers are chosen for awards. The committee will prepare a consensus report with findings and recommendations for improving the use of the center mechanism, given the many factors that must be taken into account in a specific area of re-

search, including the state of the science, presence of promising research opportunities, burden of disease, need for interdisciplinary approaches, alternative mechanisms (e.g., research project grants, program project grants, and contracts), and adequacy of the research infrastructure. The report will include recommended criteria and processes for deciding whether research centers should be created.

This report contains the results of the committee's deliberations in responding to this charge, including findings and recommendations. The report is organized around broad topics: current use of extramural centers by NIH, initiation and management of center programs, and evaluation of center programs, but each element of the charge is specifically addressed at an appropriate place in the report.

BACKGROUND ON NIH

As noted above, supporting extramural research centers within universities, medical centers, hospitals, and other research institutions is one way that NIH carries out its mission, which is "science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability."[7]

NIH itself is part of the Department of Health and Human Services, along with other health-related agencies, including the Agency for Healthcare Research and Quality, Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention (CDC), FDA, Health Resources and Services Administration, Indian Health Service, and Substance Abuse and Mental Health Services Administration. NIH is the primary federal agency for support of health *research*, accounting for more than 80 percent of annual federal expenditures on health research and development (R&D).[8]

In FY2003, NIH's budget was $27.3 billion, and the President's budget request for FY2004 would increase it to $27.8 billion.[9] Most of the budget (approximately 83 percent) funds extramural activities, including the research centers that are the subject of this report.[10] Other extramural activities include support of individual and small-group research projects, clinical trials networks, research training programs, R&D contracts, research equipment and instrumentation, and research facility construction and renova-

[7]http://www.nih.gov/about/.
[8]http://grants.nih.gov/grants/award/research/sourfund.htm.
[9]http://www.nih.gov/news/budgetfy2004/fy2004presidentsbudget.pdf.
[10]http://www.nih.gov/about/NIHoverview.html.

tion.[11] Currently, NIH is supporting about 46,000 research grants, 2,400 R&D contracts, and 17,000 research training positions at 2,000 extramural institutions.[12]

The scientific structure of NIH consists of 20 institutes and 7 centers (these centers are part of NIH itself and are not the subject of this report; they are included in the term "institutes" in the remainder of this report to avoid confusion about the term "center"). Most of the NIH institutes are focused on a disease (e.g., NCI), vital organ system (e.g., NHLBI), or population group of special concern (e.g., National Center for Minority Health and Health Disparities). Appropriations are made to the individual institutes after Congress has considered testimony from NIH officials, representatives of the scientific and medical communities, health advocacy groups, and concerned individuals. Most research grants are reviewed and scored for scientific merit by independent peer review groups that are organized by field of research (e.g., immunology) rather than disease (e.g., Parkinson's). In this way NIH attempts to ensure that the research it supports is both responding to the health needs of the public and pursuing the most promising scientific opportunities.

Support of extramural research centers has a long history at NIH. The first center program was the General Clinical Research Center Program of the National Center for Research Resources (NCRR), which began in 1959 after Congress asked NIH to improve the quality of clinical research and help move laboratory research into clinical practice more quickly. In 1960 NHLBI established the first primate research center after Congress appropriated $2 million to establish one or two such centers. In 1961 NCI began funding cancer research centers at universities and other nonprofit research institutions, and NHLBI and other institutes soon followed suit in their respective areas of research. The War on Cancer Act of 1971 mandated the establishment of "comprehensive" cancer centers, which were modeled after several leading extramural research institutions of the time that combined excellence in treatment and public education with research and training of researchers and clinicians.[13] The use of centers has grown steadily over time. NIH funded 296 center grants in 1970, 542 in 1980, and 686 in 1990.

---

[11]The intramural research program accounts for another 9 percent of the NIH budget, and the remainder funds the extramural research management and support staff, Office of the Director, National Library of Medicine, and construction and renovation of NIH buildings and facilities.

[12]Calculated from NIH table "NIH Competing and Noncompeting Research Grants by Kind and Type, FY2000" (http://grants1.nih.gov/grants/award/research/kndtyp00.txt).

[13]M.D. Anderson Hospital and Tumor Institute, Memorial Hospital and Sloan-Kettering Institute complex, and Roswell Park Memorial Institute.

CENTERS TODAY

Today, every NIH institute supports extramural centers (Appendix A). NIH reports funding 1,137 research center grants in FY2002. Although the number of extramural centers funded by NIH has grown steadily during the past 30 years, the percentage of the total NIH budget accounted for by center grants has remained between 8 percent and 9 percent since the mid-1980s. It should be noted, however, that one of the findings of this study is that some center programs use awards that are not formally classified, and therefore not counted, as center awards. This issue is addressed in Chapter 2, where recent quantitative trends in center awards are analyzed.

Many of the oldest, largest, and best known center programs fund multidisciplinary laboratory, clinical, and population-based research on a disease or other health problem with the expectation that advances in basic research will not only be facilitated in a center setting but will be translated more quickly into improved treatments there as well. These centers are also commonly expected to contribute by training new researchers and clinicians, demonstrating innovations in care in their localities, and disseminating information to health professionals and the public. Examples include the Cancer Centers, Specialized Centers of Clinically Oriented Research (in heart, lung, and blood diseases), Alzheimer's Disease Research Centers, Diabetes Research and Training Centers, and Centers for AIDS Research, which are supported by NCI, NHLBI, NIA, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and NIAID, respectively.

Congress has long favored the use of centers as a means of focusing attention on a disease it perceives as underfunded, beginning in the 1950s with the establishment of NIH's own Clinical Center and the extramural General Clinical Research Centers. In many cases, the appropriations committees have urged NIH to establish extramural research centers in reports accompanying appropriations bills, and sometimes they have specified a number of centers or earmarked an amount of funding in report language or (rarely) in the appropriations act.

From time to time, the authorizing committees establish a new center program, or codify an existing center program, by including it explicitly in the Public Health Service (PHS) Act, which means not only that NIH has to establish and fund the program but that it must go back to Congress to make major changes in the program. In recent years, the PHS Act has been amended to establish centers on Parkinson's disease (1998), autism (2000), fragile X syndrome (2000), minority health and health disparities (2000), muscular dystrophy (2001), and rare diseases (2002).

Patient advocacy groups were instrumental in persuading Congress to mandate these recent centers, which are similar in purpose to many of the earlier center programs such as the Cancer and Alzheimer's Disease Cen-

ters. They are intended to bring together basic and clinical researchers from different disciplines to focus the research on a particular disease and promote translation of the research into better treatments for patients, and they are expected to become regional resources for public information and education, clinical research training, and state-of-the-art care for patients participating in clinical research protocols.

As noted above, NIH also funds a number of other types of centers, such as centers to provide research resources (e.g., NCRR's Regional Primate Centers, Animal Resource Centers, and Biotechnology Resource Centers) or promote institutional capacity building (e.g., NCRR's Research Centers in Minority Institutions and Centers of Biomedical Research Excellence). There are also centers for multidisciplinary basic research (e.g., NIA's Nathan Shock Centers of Excellence in Basic Biology of Aging and some of NCI's Cancer Centers). Some centers were established to accelerate the development of a scientific methodology, data set, or research tool that would benefit a broad range of researchers (e.g., the Human Genome Centers set up by the National Human Genome Research Institute [NHGRI], NHLBI's Proteomics Centers, and the new Centers of Excellence in Chemical Methodologies and Library Development funded by NIGMS).

At the same time, NIH also funds activities called "centers" that are in the nature of service providers, such as data centers for clinical trials networks, but do not conduct research per se. These are usually but not always operated under contract rather than under a grant. Current examples include a Statistical and Clinical Coordinating Center for the Contraceptive Clinical Trials Network supported by the National Institute of Children and Human Development (NICHD) and a Coordinating and Biostatistics Center for the Food and Waterborne Diseases Integrated Research Network supported by NIAID. Chapter 2 examines this variety and suggests a classification scheme to better organize thinking about centers.

CONTEXT OF THIS STUDY

The immediate impetus for the congressional request for a study of centers of excellence at NIH was a question about the advisability of Congress mandating the establishment of Centers of Excellence for Muscular Dystrophy Research against the advice of NIH. The question was not an isolated one. Patient advocacy groups have pressed Congress to establish a series of center programs in recent years, and similar pressures from other advocacy groups for specific centers will no doubt be proposed in the future.

Immediate Context

NIH was directed to expand research on muscular dystrophy by the Children's Health Act of 2000, which had a brief section that said little more than that "The Director of NIH shall expand and increase coordination in the activities of the National Institutes of Health with respect to research on muscular dystrophies, including Duchenne muscular dystrophy" (DMD) and that "There are authorized to be appropriated such sums as may be necessary to carry out this section."[14] The bill addressed a number of childhood diseases and mandated five autism and three fragile X syndrome centers, but when it was discussed on the floor, a number of members of the House commented that NIH was not doing enough about muscular dystrophy. NIH responded by holding a workshop in May 2000 on DMD and issuing a new Program Announcement (PA), "Research on Therapeutic and Pathogenic Approaches for the Muscular Dystrophies," in January 2001 soliciting research proposals from extramural scientists. NIH also sponsored a conference on facioscapulohumeral muscular dystrophy in May 2000 and issued an RFA soliciting exploratory research on the disorder in November 2000.

In February 2001, at the urging of muscular dystrophy patient advocacy groups, Representative Roger Wicker introduced H.R. 717, the Duchenne Muscular Dystrophy Childhood Assistance, Research and Education Amendments of 2001. The bill called for expansion of research and related programs concerning DMD and establishment of at least three DMD "centers of excellence" by NIH, establishment of three regional centers of excellence in DMD epidemiology by CDC, and establishment of an interagency muscular dystrophy coordinating committee to prepare a plan and report annually to Congress.

Two weeks later, the Senate Appropriations Subcommittee on Labor, Health and Human Services, and Education held hearings on muscular dystrophy. Jerry Lewis, chairman of the Muscular Dystrophy Association (MDA), and Dr. Leon Charash, chair of MDA's Medical Advisory Committee, testified that, while MDA had funded most of the advances in knowledge to date about muscular dystrophy and the genetic defects causing it, turning that knowledge into effective therapies was going to be so expensive that federal funding would be needed. The president of Parent Project for Muscular Dystrophy Research and its scientific director testified that NIH funding was small and hardly growing and endorsed centers to provide an environment in which a critical mass of researchers could be assembled and promote more rapid translation of research into treatments.

[14]P.L 106-301, Children's Health Act of 2000, Title XXII, Muscular Dystrophy Research.

In May 2001 Senator Paul Wellstone introduced S. 805, a bill similar to the House bill, except that it broadened the focus of research to include all muscular dystrophies.[15] To handle the broader scope, the bill increased the number of mandated centers from three to five.

The House Subcommittee on Health held hearings on H.R. 717, dubbed the MD-CARE Act, in June 2001. Subcommittee members and patient advocates testified that NIH was not doing enough and called for a greater effort in developing therapies and clinical trials. Representative Charles Pickering, one of the bill's sponsors, noted the January 2001 PA setting aside $5 million over five years and said, "This is a positive development but more needs to be done. NIH must reorder its priorities to assure that developments in therapies to treat this disease are translated to clinical trials and to the patients."[16] When the bill was marked up by the House Energy and Commerce Committee several weeks later, Chairman W.J. "Billy" Tauzin released a statement that the legislation authorized Centers of Excellence for Muscular Dystrophy "so that extramural research supported by NIH will bring some focus to this disease."

NIH's position was that too little was understood about muscular dystrophies to justify the costs of clinically oriented centers. It argued that expanded funding should be used to support individual-investigator grants to advance the state of the science to the point that more elaborate programs, such as program projects, and eventually centers, would be productive. There were concerns that there might not be five good proposals and that center grants would most likely go to the small cadre of top investigators in the field who were already funded through individual project grants rather than expand the pool of researchers. NIH was also worried about the expectations of patient groups that research centers would also be treatment centers, because NIH's mission does not include treatment except for the limited number of patients involved in clinical protocols. Advocacy groups for dystrophies that were less studied than DMD were also concerned about a premature emphasis on centers. During the hearing, Representative Wicker thanked the scientists from NIH "who helped us refine the

[15]Although Duchenne is the most common, others include myotonic dystrophy, facioscapulohumeral muscular dystrophy, the limb-girdle muscular dystrophies, Emery-Dreifuss muscular dystrophy, and congenital muscular dystrophy.

[16]Representative Pickering, at the hearing on the proposed legislation by the House Subcommittee on Health on June 27, 2001. In addition to centers, the bill included language directing the NIH director, in coordination with the directors of National Institute of Neurological Diseases and Stroke (NINDS), NIAMS, NICHD, and other institutes, to "expand and intensify programs of such institutes with respect to research and related activities concerning various forms of MD," and provisions for an interagency MD Coordinating Committee to develop a research plan and report biennially to Congress on progress, a National MD Epidemiology Program by CDC, and a program of public and professional information and education.

language to make it more workable." The bill reported to the floor still required centers of excellence but did not specify a number, and the scope of the bill was broadened to address all muscular dystrophies.[17]

The Senate Subcommittee on Health heard the same arguments from NIH as the House committee did. NIH said that legislation that did not specify the number of centers was an improvement, but it still did not think that centers were the best use of funds for research on muscular dystrophy. For its part, the subcommittee was concerned about what seemed to be a growing trend among advocacy groups to consider centers a key element of every research program, regardless of differences in the state of knowledge about the disease in question. This concern was probably reinforced by the initial draft of the MD-CARE Act, which appeared to be little more than the earlier bill for autism research, including centers of excellence, in the Children's Health Act of 2000, but with "muscular dystrophy" substituted for "autism" wherever it appeared.

A related problem was the difficulty experienced by NIH in conveying to the subcommittee how it determines if and when centers are appropriate vehicles to support research. The decision to establish a center program is, according to NIH, a complicated judgment. Among other factors, it is based on the specific state of the science involved, including whether there are promising research opportunities and enough qualified investigators to take the lead. This complexity makes it more difficult for Congress to judge the merits of requests for centers from advocacy groups (or other members of Congress). The subcommittee added a section to the bill that required NIH to go to the IOM "for the purpose of conducting a study and making recommendations on the impact of, need for, and other issues associated with Centers of Excellence at the National Institutes of Health." The amendment was accepted in both houses and the MD-CARE Act was signed into law on December 18, 2001.

Broader Context

The interactions among Congress, NIH, and the voluntary associations lobbying on behalf of muscular dystrophy patients and their families might

[17]Subsequently, the Senate Labor-HHS Appropriations Subcommittee, in its report on the FY2002 appropriations for NIH, "strongly" urged NINDS "to establish no fewer than three centers of excellence for basic and applied research in the muscular dystrophies." The report also called for "meaningful implementation" of the new centers of excellence in autism research mandated in the Children's Health Act of 2000. In October 2003 NIH announced the establishment of three cooperative research centers for the muscular dystrophies and plans to establish two more. NIH funded two Autism Research Centers of Excellence in May 2002 and seven more in September 2003.

never have led to the present study had the MD-CARE bill been an isolated case, but as noted above, it was perceived to be part of a larger trend. In 1997, for example, advocates for more research on Parkinson's disease lobbied for legislation authorizing a $100 million program consisting of research centers, training grants, a patient information center, and other mechanisms. NIH director Harold Varmus testified against the bill, telling the Senate Committee on Labor and Human Resources that advances were more likely to come from basic research than from Parkinson's-specific research, and that NIH could not "responsibly fund" the 10 Parkinson's Disease Research Centers of Excellence called for in the bill (Wadman, 1996).[18] The support for the Udall bill was so strong that when the effort to pass a reauthorization bill foundered over disputes about use of fetal tissue, the Parkinson's program was added to the PHS Act by including it in the Labor-Health and Human Services-Education appropriations act.

Bills specifying not less than five "centers of excellence regarding research on autism" and for at least three "centers to conduct research for the purposes of improving the diagnosis and treatment of, and finding the cure for, fragile X" were folded into the Children's Health Act of 2000.[19] NIH argued against the autism centers on the grounds that the field was not advanced enough to warrant centers, and that the Collaborative Programs of Excellence in Autism, a multisite cooperative research network established in 1997 and funded by the program project grant mechanism, was the more appropriate mechanism for pushing research on autism beyond the R01 stage. There was concern that having to fund five centers in short order would mean that those already working in the field, whose best ideas were already funded, would be most likely to compete successfully for center grants, and that the net gain in effectiveness would be less than using the funding to increase the number of individual project grants, which would be more likely to attract new talent into the field. Congress was not convinced, and the five centers were mandated.

In the last session of Congress, several bills included research centers, and one was passed into law. The Rare Diseases Act of 2002 authorizes the director of the NIH Office of Rare Diseases to fund "regional centers of excellence for clinical research into, training in, and demonstration of diagnostic, prevention, control, and treatment methods for rare diseases."[20]

Each of these cases posed the question: When is it appropriate to estab-

[18]The centers, called Morris K. Udall Parkinson's Disease Research Centers of Excellence after the congressman who died of the disease in 1998, were established in 1998 and 1999.

[19]P.L. 106-310, October 17, 2000.

[20]P.L. 107-280, November 6, 2002. On November 3, 2003, NIH announced the establishment of seven Rare Diseases Clinical Research Centers and a Data and Technology Coordinating Center.

lish a center program as part of NIH's portfolio of extramural activities addressing a particular problem? This report examines the program planning procedures NIH uses to decide on whether to initiate a new extramural center or other program and recommends ways to clarify and improve the process and criteria for determining whether to establish centers.

METHODS OF THE PRESENT IOM STUDY

In the autumn of 2002, IOM assembled a committee whose members provided expertise in the fields of basic, clinical, and population research; research administration; grants management; center administration; evaluation of research programs; patient advocacy; health education/research training; biostatistics; and voluntary health association management. Members also have a wide range of experiences participating in centers supported by NIH and other federal agencies. This was accomplished in accordance with the established procedures of the National Academies, including examining possible biases and conflicts of interest and providing an opportunity for public comment. Brief biographies of the committee members are provided in Appendix B.

The committee used a wide variety of sources to assemble the data and information necessary to respond to its charge. An initial organizational meeting of the committee in December 2002 provided an opportunity to explore the parameters of the study with the study sponsor, the NIH Office of Extramural Research. The meeting also gave the committee time to discuss a background paper by Michael McGeary on the history and current status of NIH center grant programs, which formed the basis of Chapters 1 and 2 of this report.

At a subsequent meeting, in February 2003, the committee learned details of the legislative and NIH origins of a wide variety of center programs. Present and former institute directors provided their views on the pluses and minuses of centers as a means of advancing research, as did the president of a major medical center, dean of a leading school of nursing, president of the National Health Council, president of the Association of Academic Health Centers, president of the Federation of American Societies for Experimental Biology, and representatives from the Association of American Medical Colleges, Association of Professors of Medicine, American Psychological Association, American Society for Nutritional Sciences, Association of Population Centers, and American Autoimmune-Related Diseases Association. The director of program development for the Agency for Healthcare Research and Quality described her agency's model for evaluating the impact of medical research, and the leader of the health team of the staff of the Senate Committee on Health, Education, Labor, and Pensions explained the committee's reasons for mandating this study.

IOM staff advertised widely for input from scientific and professional societies, voluntary health associations, and other interested groups and individuals, and received written responses from 11 additional groups. In addition, IOM staff conducted telephone interviews with the NIH scientists listed as points of contact for 12 center programs for which RFAs were published in 2002 and 2003. These interviews focused on the circumstances surrounding the origins and decision-making processes underlying these RFAs as well as plans for managing and evaluating the programs when they were implemented.

The sponsor's project officers compiled and provided several custom reports on the number and funding of center programs as additional sources of information. The committee members themselves contributed both personal contacts and specific information from their own files and experience. The NIH website provided much information about specific center programs, institute-specific analyses and evaluations of center programs, and responses to laws and legislative language. Project staff examined all center-related RFAs and PAs published in 2002 and the first two months of 2003 for information on the genesis and purpose of each center program and contacted NIH program staff for clarification and additional information, as necessary.

The present report was the result of extensive discussion among the committee members at two-day meetings in April, June, and August 2003, during which the committee discussed and drafted answers to each of the specific questions specified in P.L. 107-84 in its charge to the committee. Revisions were reviewed and modified via e-mail, and committee members signed off on the review draft in August 2003. After review by a panel of independent reviewers and attendant revisions to the manuscript, the report was released in February 2004.

ORGANIZATION OF THE REPORT

The remainder of this report is organized into chapters that address the major issues: What are centers and what are their unique contributions or added value in achieving NIH's goals? (Chapter 2); How are center programs initiated and managed? (Chapters 3 and 4); How should centers and center programs be evaluated? (Chapter 5); and closing comments (Chapter 6). Several appendixes provide further information about the committee and NIH Center programs.

REFERENCES

Finkelstein JS, Hayes A, Hunzelman JL, Wyland JJ, Lee H, Neer RM. 2003. The effects of parathyroid hormone, alendronate, or both in men with osteoporosis. *New England Journal of Medicine* 349(13):1216-1226.

IOM and NRC (Institute of Medicine and National Research Council). 2003. *Large-Scale Biomedical Science: Exploring Strategies for Future Research*. Washington, DC: The National Academies Press.

MIT (Massachusetts Institute of Technology). 2003. *Philanthropists Eli & Edythe Broad of Los Angeles Give $100M to Create Institute with MIT, Harvard, and Whitehead to Fulfill Genome's Promise for Medicine* (Press Release). Center for Genome Research, Whitehead Institute, MIT, Cambridge, MA. [Online]. Available: http://www.genome.wi.mit.edu/broad/ [accessed December 15, 2003].

NHLBI (National Heart, Lung, and Blood Institute). 1996. *Minutes of the April 19 Meeting of the NHLBI Special Emphasis Panel on Integrative Research*. [Online]. Available: http://www.nhlbi.nih.gov/meetings/workshops/intphys.txt [accessed December 15, 2003].

NIA (National Institute on Aging). 2001. *Guide to Research and Training Programs*. [Online]. Available: http://www.nia.nih.gov/about/niaguide.pdf [accessed June 26, 2003].

NIGMS (National Institute of General Medical Sciences). 1998. *Minutes of the May 1998 Meeting of the Advisory Council* [Online]. Available: http://www.nigms.nih.gov/about_nigms/council_may98.html [accessed December 15, 2003].

NIH (National Institutes of Health). 2003. *Congressional Budget Justification for FY2004*. [Online]. Available: http://www4. od.nih.gov/officeofbudget/FY04pubs/Overview.pdf [accessed December 15, 2003].

OAR (Office of AIDS Research). 1999. *Report to the Director, Office of AIDS Research, of the Focus Group to Review the Centers for AIDS Research (CFAR) Program*. [Online]. Available: http://www.nih. gov/od/oar/public/CFARrpt090899.pdf [accessed December 15, 2003].

Steinberg MH, Barton F, Castro O, Pegelow CH, Ballas SK, Kutlar A, Orringer E, Bellevue R, Oliveri N, Eckman J, Varma M, Raqmirez G, Adler B, Smith W, Carlos T, Ataga K, DeCastro L, Bigelow C, Sauthararajah Y, Telfer M, Vichinsky E, Claster S, Shurin S, Bridges K, Waclawiw M, Bonds D, Terrin M. 2003. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: Risks and benefits up to 9 years of treatment. *Journal of the American Medica Association* 289(13):1645-1651.

Wadman M. 1996. NIH resists bill to promote research into Parkinson's [News]. *Nature* 381:542.

Zerhouni E. 2003a. Opening Statement on the FY2004 President's Budget Request, "FY 2004 Appropriations Overview," Hearing before the House Appropriations Subcommittee on Labor, Health and Human Services, and Education, April 2, 2003. [Online]. Available: http://www.nih.gov/about/director/budgetrequest/FY2004budgetrequest.htm [accessed December 15, 2003].

Zerhouni E. 2003b. NIH Announces Strategy to Accelerate Medical Research Progress (Press Release). [Online.] Available: http://www.nih.gov/news/pr/sep2003/od-30.htm [accessed December 15, 2003].

2

Current Use of Center Awards

The National Institutes of Health (NIH) has long tracked its budget by "mechanism," one of which is research centers. Other mechanisms include research project grants (RPGs), other research grants, research and development (R&D) contracts, research training, and intramural research. Three of the budget mechanisms—RPGs, research centers, and other research grants—account for two-thirds of NIH's total budget. Table 2-1 is a simplified version of the mechanism table submitted with NIH's fiscal year (FY) 2003 budget request.

As a first approximation of the use of centers by NIH, administrative data on the numbers and amounts of research center awards reported by NIH are analyzed in the first section of this chapter. These data are based on the coding system NIH uses to keep track of extramural awards, in which certain grants and cooperative agreements are coded as center awards. A later section of the chapter discusses the fact that NIH's coding of center grants leaves out a relatively small but growing, and perhaps important, set of awards that appear to support centers but are not coded as center awards in NIH's budget and extramural award statistics.

OVERALL NUMBER, COST, AND LOCATION OF NIH CENTER AWARDS

In February 2003, when NIH submitted its FY2004 budget request to Congress, it estimated that it would fund 1,209 research center awards in FY2003 at a cost of $2.4 billion per year. The actual number of centers is

somewhat smaller than the number of awards, because the same site may receive multiple awards and competitive supplements. NIH does not track the number of centers, but the committee estimates that the unduplicated number of entities with center awards is approximately 1,050 after supplements and multiple awards are accounted for.

Figure 2-1 graphically displays the number of center grants awarded in each state in FY2002. There were center grants in every state. California, with 179, was the state holding the most center grants in FY2002, followed by Massachusetts with 97. The median number of center awards among the states was 16. This distribution is generally in line with the overall distribution of NIH extramural awards of all kinds.

Funding for center grants has generally increased in line with the overall NIH budget in recent years, constituting between 8 percent and 9 percent of the total NIH budget during the 1992 to 2003 period (Figure 2-2). In FY2002 the average center grant was $1.9 million a year. The range spanned three orders of magnitude however, from $55 thousand to $56 million, and the median annual center grant amount was only $1.3 million.

The FY2004 budget request sought an increase of $167 million to fund 1,237 center grants in FY2004 (see Table 2-1). If the proposed budget

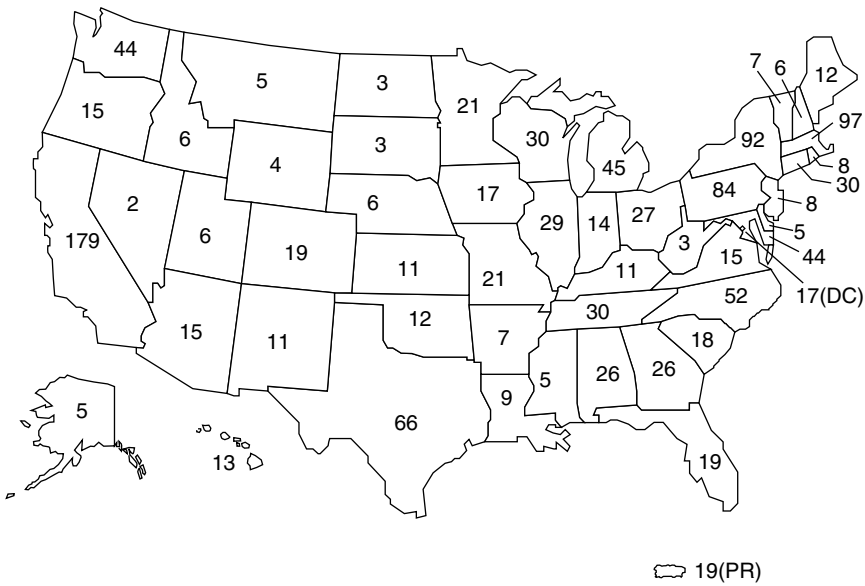

FIGURE 2-1 Distribution of research center awards by state, FY2002.
SOURCE: Based on data provided by NIH Office of Extramural Research, April 16, 2003.

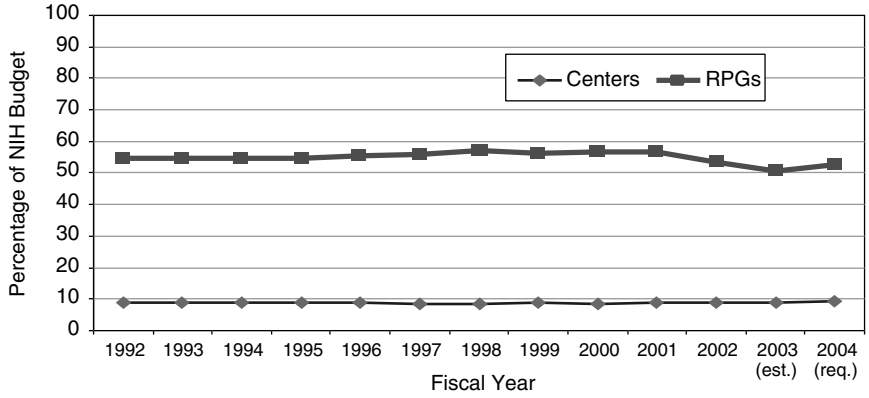

FIGURE 2-2 Center and research project grant (RPG) funding as percentage of NIH budget, FY1992-FY2004.
SOURCE: NIH mechanism table in FY2004 Congressional Justification Budget (U.S. DHHS, 2003).

increase is approved by Congress, center awards would constitute 9.3 percent of the FY2004 NIH budget, compared with 9.0 percent in 2000 and 8.9 percent in 2001.

The increase in the funding of center awards since FY1992 has been approximately the same as the increase in funding for RPGs and for all research grants during the same period. There has been more of a change in the size of center grants because the number of center awards has not grown as fast as the funding. Assuming the FY2004 budget is approved, the number of center awards will have increased by 43 percent since FY1992 (from 868 to 1,237) while funding increased by 133 percent in real (i.e., inflation-adjusted) terms. In 2004 dollars, the mean center grant was $1.3 million in FY1992 and will be $2.1 million, or 64 percent larger, in FY2004.

TRENDS BY INSTITUTE

The National Center for Research Resources (NCRR), perhaps a special case because of its mission to provide research resources, funded the most center awards in FY2001, 313 (approximately 25 percent of the total). The National Cancer Institute (NCI) led the remaining institutes, with 140 center awards, and the National Heart, Lung, and Blood Institute (NHLBI) came in third, with 81 (Table 2-2). The National Institute on Drug Abuse funded 33, the median number of center awards among the institutes.

From FY1992 to FY2001 the biggest growth in number of center

TABLE 2-1 NIH Budget by Mechanism (in millions of current dollars)

Mechanism	FY2002 (Actual)		FY2003 (Estimated)		FY2004 (Requested)	
	Number of Awards	Amount of Funding	Number of Awards	Amount of Funding	Number of Awards	Amount of Funding
Research Project Grants	36,231	13,017.0	38,309	14,298.1	39,520	15,203.8
Research Centers	1,137	2,116.9	1,209	2,422.4	1,237	2,589.0
Other Research Grants	5,915	1,446.1	6,213	1,608.9	6,348	1,662.2
Subtotal, Research Grants	43,283	16,580.0	45,731	18,329.4	47,105	19,455.0
Training Awards		653.3		693.2		715.5
R&D Contracts	1,999	1,797.0	2,397	2,430.4	2,438	2,779.0
Intramural Research		2,234.0		2,548.8		2,629.8
Research Mgt. & Support		785.9		920.1		968.8
Cancer Prevention & Control		486.6		539.8		551.8
Extramural Construction		117.6		457.0		0
National Library of Medicine		274.3		305.9		316.0
Office of the Director		253.5		274.0		318.0
NIH Buildings and Facilities		295.9		769.1		80.0
TOTAL		23,478.1		27,267.6		27,814.0

SOURCE: The data on which this table is based come from NIH's FY2004 Congressional Justification Budget (U.S. DHHS, 2003). The key table is posted on the NIH website at http://www.nih.gov/news/budgetfy2004/fy2004presidentsbudget.pdf.

TABLE 2-2 Number of Center Awards by Institute, FY1992-FY2001

	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	Percent change, 1992-2001
NIAAA	13	14	13	15	16	15	14	17	15	15	15.4
NIA	51	55	63	66	60	72	66	61	65	66	29.4
NIAID	27	10	14	14	14	14	22	14	17	19	–29.6
NIAMS	25	26	31	31	29	26	27	37	29	37	48.0
NCCAM								10	16	14	NA
NCI	87	101	157	78	68	68	64	94	94	140	60.9
NIDA	25	23	34	36	30	30	32	33	34	33	32.0
NIDCD	17	16	15	16	16	18	17	17	17	19	11.8
NIDR	28	28	29	27	32	48	21	19	15	13	–53.6
NIDDK	48	61	59	59	59	57	58	65	68	69	43.8
NIEHS	18	19	22	23	24	22	25	27	27	26	44.4
NEI	29	29	30	30	31	32	33	34	37	39	34.5
NIGMS	11	10	8	10	10	9	7	9	17	26	136.4
NICHD	77	78	78	68	69	70	75	76	73	63	–18.2
NHGRI	15	14	12	12	14	16	13	20	21	26	73.3
NHLBI	65	68	68	75	78	77	82	82	81	81	24.6
NIMH	53	56	60	57	55	55	54	57	57	52	–1.9
NINR	7	7	7	6	6	7	7	9	10	19	171.4
NINDS	42	46	44	43	39	38	38	46	48	50	19.0
NCRR	230	238	241	267	278	265	257	262	283	313	36.1
All	868	899	985	933	928	939	912	989	1024	1120	29.0
All except NCRR	638	661	744	666	650	674	655	727	741	807	26.5

SOURCE: Unpublished table of Information for Management, Planning, Analysis, and Coordination (IMPAC) data provided by NIH Office of Extramural Research, October 29, 2002.

awards was at NCRR (83 more centers), NCI (53 more), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) (21 more), and NHLBI (15 more), which together accounted for two-thirds of the net gain of 253 centers during the period. Although NCRR's total increased by 83 (most of them developmental grants for the Institutional Development Award [IdeA] program, discussed below), the base was large, and so the percentage increase was a modest 36 percent. The National Institute of Nursing Research (NINR) had the biggest percentage gain in number of centers (171 percent), followed by the National Institute of General Medical Sciences (NIGMS) (136 percent) and the National Human Genome Research Institute (NHGRI) (73 percent).

The pattern of funding was similar to that of the number of center awards (Table 2-3). NCI spent the most on centers in 2001, but NHGRI spent the second largest amount, followed by NHLBI. From 1992 to 2001, NIGMS increased its funding of centers the most, by 936 percent in real terms. NHGRI was second at 587 percent, followed by NINR at 212 percent (the mean was 74 percent, the median 39 percent, excluding NCRR). In absolute terms, NHGRI had the largest gain from 1992 to 2001, $211 million, followed by NCI and NIGMS. Those three institutes accounted for 75 percent of the net increase in funding over the period.

The relationship of the centers to their institutes is another matter, at least as measured by their share of the budget. NCI spends the most of any institute on centers, but centers still account for only 6.9 percent of NCI's overall budget (Figure 2-3). Only four institutes expended more than 10

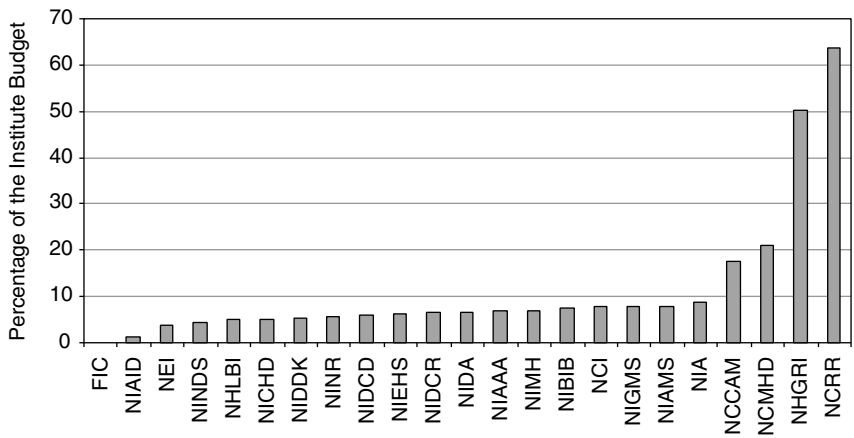

FIGURE 2-3 Center funding as a percentage of the institute's budget, FY2002.
SOURCE: Institute mechanism tables in the FY2004 Congressional Justification Budget (U.S. DHHS, 2003).

TABLE 2-3 Funding of Center Awards, by Institute, FY1992-FY2001 (in millions of dollars)

Institute	1992	1993	1994	1995	1996	1997	1998
NIAAA	$16.8	$17.3	$18.8	$19.9	$21.1	$21.9	$22.3
NIA	$45.3	$51.5	$55.4	$58.3	$58.6	$61.7	$64.9
NIAID	$14.8	$7.7	$9.6	$9.8	$10.4	$10.3	$14.6
NIAMS	$22.5	$23.6	$25.8	$26.1	$25.2	$24.8	$27.5
NCCAM	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
NCI	$145.1	$145.0	$158.7	$155.7	$162.3	$159.9	$163.5
NIDA	$24.1	$26.6	$39.0	$41.4	$41.1	$42.1	$43.0
NIDCD	$16.3	$17.1	$16.7	$16.3	$16.6	$18.0	$18.6
NIDR	$18.5	$18.1	$19.7	$21.5	$22.9	$25.7	$23.2
NIDDK	$40.6	$46.7	$51.4	$52.9	$52.7	$54.5	$56.9
NIEHS	$16.9	$18.1	$20.6	$21.4	$22.1	$23.6	$23.3
NEI	$7.6	$7.6	$8.1	$8.3	$9.0	$9.8	$11.2
NIGMS	$7.4	$7.8	$7.0	$8.3	$9.0	$8.9	$6.7
NICHD	$49.9	$49.0	$48.5	$47.6	$46.8	$51.4	$55.7
NHGRI	$29.4	$31.4	$33.0	$38.0	$42.7	$53.8	$74.2
NHLBI	$96.5	$96.8	$101.5	$107.0	$108.2	$110.2	$117.2
NIMH	$63.8	$65.3	$69.6	$68.3	$68.9	$72.3	$74.0
NINR	$1.7	$1.8	$1.8	$1.9	$2.1	$2.9	$3.0
NINDS	$31.5	$31.2	$35.5	$39.2	$38.6	$36.6	$40.9
NCRR	$245.9	$247.9	$264.9	$278.6	$291.5	$312.9	$335.3
All	$894.4	$910.6	$985.5	$1,020.7	$1,049.9	$1,101.3	$1,175.8
All except NCRR	$648.5	$662.6	$720.6	$742.1	$758.4	$788.4	$840.6

SOURCE: Unpublished table of IMPAC data provided by NIH Office of Extramural Research, October 29, 2002 (the factor used to determine real change was the gross domestic product (GDP) implicit price deflator, from Table 10.1 in OMB, 2003).

percent of their budget on center awards. Both NCRR and NHGRI spent more than half their budgets on center awards.

TRENDS BY ACTIVITY CODE

NIH also uses a set of "activity codes" to track its expenditures that is more detailed than the budget mechanism categories. There are 13 budget mechanisms, but there are several hundred activity codes. The best-known activity code is R01, which denotes the traditional individual investigator-initiated RPG. Other commonly used activity codes are R21 (exploratory/developmental grants), R03 (small research grants), U01 (research project cooperative agreements), K01 (research scientist development awards), and P01 (research program projects).

			Nominal change 1992-2001		Real change 1992-2001	
1999	2000	2001	Amt.	Percent	Amt.	Percent
$24.0	$24.2	$25.0	$8.2	48.6	$4.9	24.7
$70.9	$72.3	$75.0	$29.6	65.4	$20.9	38.8
$15.9	$19.4	$22.7	$7.9	53.4	$5.1	28.7
$30.2	$29.1	$32.0	$9.4	41.9	$5.1	19.1
$13.4	$21.7	$20.8	$20.8	NA	$20.8	NA
$206.5	$242.9	$299.9	$154.7	106.6	$126.9	73.3
$45.9	$47.7	$47.0	$22.9	95.4	$18.3	63.9
$19.1	$16.4	$16.0	-$0.3	–2.1	–$3.5	–17.9
$23.8	$24.4	$24.1	$5.6	30.2	$2.0	9.2
$63.7	$67.0	$76.1	$35.6	87.7	$27.8	57.4
$27.6	$29.3	$31.6	$14.7	86.6	$11.4	56.5
$13.0	$14.8	$17.9	$10.2	133.5	$8.7	95.9
$7.4	$49.8	$91.1	$83.7	1135.0	$82.3	936.0
$59.1	$60.7	$60.6	$10.7	21.4	$1.1	1.9
$139.4	$170.1	$240.5	$211.2	719.5	$205.6	587.4
$122.4	$123.8	$126.7	$30.2	31.3	$11.7	10.1
$81.3	$78.5	$75.5	$11.7	18.4	–$0.5	–0.7
$3.0	$4.0	$6.2	$4.5	271.3	$4.2	211.5
$53.7	$58.9	$59.8	$28.4	90.2	$22.3	59.5
$388.9	$435.5	$588.2	$342.3	139.2	$295.0	100.6
$1,408.9	$1,590.6	$1,936.4	$1,042.0	116.5	$870.1	81.6
$1,020.0	$1,155.1	$1,348.3	$699.7	107.9	$575.1	74.4

The activity codes constituting the research center mechanism, and their definitions, are provided in Appendix B. The predominant codes for research center awards are P30 core grants, P50 and U54 specialized centers, and P60 comprehensive centers. Specialized centers were the most numerous in 2001 (383). Core grants were second in number (318), and there were far fewer comprehensive centers (44) (Figure 2-4). Growth rates were similar over the 1992 to 2001 period, with specialized centers constituting about 34 percent of the group in 1992 and 2001, core grant centers about 27 percent and 28 percent, and comprehensives 5 percent and 4 percent, respectively.

In terms of dollars awarded, specialized centers had the most funding and the fastest growing budgets (Figure 2-5). Their share of the funding for the three main center types grew from 54 percent in 1992 to 64 percent in

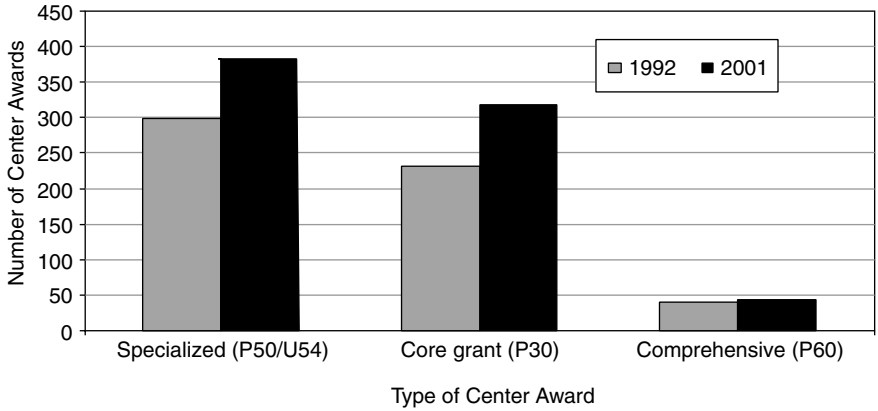

FIGURE 2-4 Number of specialized, core, and comprehensive center awards, FY1992 and FY2001.
SOURCE: Unpublished table of IMPAC data provided by the NIH Office of Extramural Research, October 29, 2002.

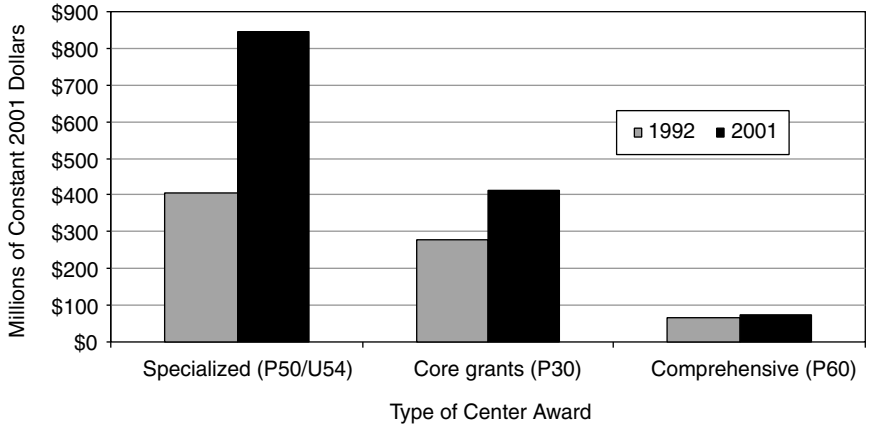

FIGURE 2-5 Funding of specialized, core, and comprehensive center awards, FY1992 and FY2001 (in constant dollars). The factor used to calculate constant dollars is the GDP implicit price deflator, from Table 10.1 in OMB, 2003.
SOURCE: Unpublished table of IMPAC data provided by the NIH Office of Extramural Research, October 29, 2002

2002. The comparable shares for core grant centers were 37 percent and 31 percent, and for comprehensive centers they were 9 percent and 6 percent, respectively.

Among the other types of centers (not shown), one big change was in the number of P20 planning or developmental awards, primarily because of

growth in the NCRR IdeA program.[1] The number of P20 grants in 2001 was double the number in 1992 (120 compared with 62). Most of the new P20s in 2001 were supported by NCRR and NCI, and most of the increase in funding was by NCRR, because its new P20 grants averaged more than $2.5 million compared with less than $300,000 for new P20 grants awarded by other institutes. This trend will be reinforced by the longer length of IdeA P20s being awarded by NCRR—three to five years instead of the usual one year. However, the funding involved was still relatively small—$135 million in FY2001.

In constant dollars, funding for P50/U54 specialized centers increased by 110 percent from 1992 to 2001, compared with 48 percent and 12 percent for core grant centers and comprehensive centers, respectively. Several factors help explain the large relative increase in funding of specialized centers. NHGRI spending on centers went from $30 million to $240 million, and almost all of it was for specialized centers. NCI launched the Specialized Programs of Research Excellence program (SPOREs) in the early 1990s, which is funded by P50 grants, and NCI spent $100 million on SPOREs in 2001, compared with $16 million in 1992. The two institutes accounted for 57 percent of the net increase in the funding of specialized centers from 1992 to 2001. The increase in funding of specialized centers was apparently determined by NIH, because neither the NHGRI nor NCI SPORE centers were established at the urging of advocacy groups or mandated by Congress.

Given these trends, it is no surprise to find that the average size of awards for specialized centers increased greatly relative to P30 core grants and P60 comprehensive centers (Figure 2-6). In constant dollars, awards for specialized centers were $2.2 million a year on average in 2001, compared with $1.4 million in 1992. The average core grant was almost as big as the average specialized center grant in 1992, at $1.2 million in 2001 dollars, but it only increased to $1.3 million in 2001. The average comprehensive center award hardly grew in real terms either. It was $1.65 million in 1992 and $1.68 million in 2001.

Although not shown here, funding of the Primate Research Centers also increased sharply in real terms from 1992 to 2001, from $3.6 million a year per center, on average, to $7.5 million a year per center in 2001 dollars, but overall funding only went from $50 million to $60 million

[1]The IdeA P20 center program is open to institutions in the 24 states that received less than $70 million from NIH, or had success rates of less than 20 percent for grant applications to NIH, in a recent five-year period. The program funds Centers of Biomedical Research Excellence (COBREs) and Biomedical Research Infrastructure Networks (BRINs) with P20 developmental center grants.

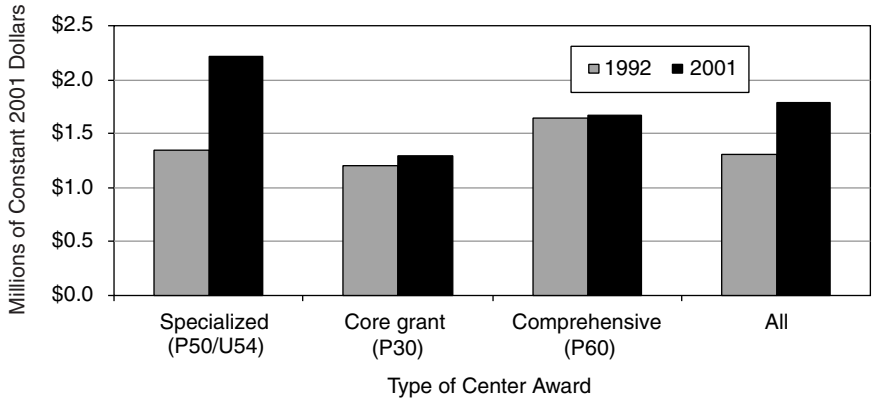

FIGURE 2-6 Average size of specialized, core, and comprehensive center awards, FY1992 and FY2001 (in constant dollars). The factor used to calculate constant dollars is the GDP implicit price deflator, from Table 10.1 in OMB, 2003.

because the number of centers was consolidated from 14 to 8. P20 grants also increased in size, from $323,700 a year in 1992 to $1.2 million a year in 2001 (259 percent), in 2001 dollars.

SUMMARY OF NIH DATA ON NUMBER AND COST OF CENTER GRANTS

NIH funded 1,120 research center grants in FY2001, at a cost of $1.9 billion. This was about 9 percent of the NIH budget. Most institutes allocated a smaller percentage of their budget to centers (the median was 6.9 percent), while a few, notably NCRR and NHGRI, devoted much more and drove up the mean. After accounting for inflation, funding of centers increased 82 percent from FY1992 to FY2001. Because this was roughly the same rate of increase as in the NIH budget as a whole, the share of NIH funding devoted to center grants did not increase appreciably over that period. If the President's budget request for FY2004 is enacted, centers will increase their share of the NIH budget slightly, from an estimated 8.9 percent in FY2003 to 9.3 percent.

There have been internal shifts in the center awards category, however, including an expansion of NCRR funding of centers relative to the other institutes (from 28 percent to 36 percent of all center funding from 1992 to 2001), and the emergence of NHGRI as a major supporter of centers. In fact, if NCRR and NHGRI are excluded from the calculation, funding for centers grew by only 37 percent in constant dollars between 1992 and 2001.

COMPARISON OF CENTER AWARDS TO OTHER FORMS OF RESEARCH FUNDING

NIH uses a number of funding mechanisms to support a variety of research and related activities in the nation's research institutions as part of its mission to improve health through research on basic processes of health and disease and on ways to turn new knowledge into better treatments and other applications. Approximately 83 percent of the NIH budget is devoted to such extramural research (9 percent supports the intramural research program and the rest funds the National Library of Medicine, program staff in the institutes, Office of the Director, and construction of NIH facilities, activities that are outside the scope of this report).[2]

The extramural program funds basic and applied biomedical and behavioral research, research training, and career development. These activities are carried out in many ways, most commonly by individual investigators working on specific projects, small groups of investigators with related projects, multidisciplinary centers focused on a particular problem or set of questions, and groups or networks of investigators conducting clinical research according to common protocols. NIH also supports research resources and facilities through national and regional centers.

The funding mechanisms that NIH employs (see Table 2-1) roughly correspond to the main modes of research. RPGs mostly support individual researchers and small research groups. Center awards support interdisciplinary research centers and research resource centers. Other research grants are used for several purposes, with most of the funding going to career development (K-series) grants and cooperative clinical research groups (U10). Training awards go to academic institutions and to individual graduate students and postdoctoral fellows.

NIH, with some variation among institutes, awards the largest number of grants (including cooperative agreements) and highest amount of grant funding to individual investigators. The basic individual-investigator grant, the R01, accounted for nearly half (47 percent) of the budget for extramural research in FY2002 (Table 2-4). Program project grants, P01s, which go to small groups of several investigators for projects with the same theme, accounted for 7 percent of extramural funding. U01, U19, and U10 cooperative agreements, commonly used to support clinical trials and clinical research groups and networks spanning a number of medical centers, accounted for 9 percent. Center awards accounted for 11.5 percent of the budget for extramural research. These shares have not changed much since

[2]For the distribution of the NIH budget in FY2003, see http://grants1.nih.gov/grants/ward/trends/distbud02.htm.

TABLE 2-4 NIH Extramural Research Mechanisms, FY2002

Mechanism	Activity Code	Number of Extramural Awards	Amount of Extramural Funding	Percentage of All Extramural Funding
Research Project Grants	All	34,613	$12,623,765,090	66.2
	R01	27,568	$8,985,081,987	47.1
	P01	993	$1,383,021,764	7.3
	U01, U19	1,271	$1,339,073,659	7.0
	Other	4,856	$1,017,255,905	4.8
Small Business Programs	All	1,893	$497,433,378	2.6
Centers	All	1,261	$2,198,971,367	11.5
	P30 Core	317	$438,867,746	2.3
	P50, P60, U54 Research Resource Centers	472	$1,014,240,236	5.3
	Other (P20)	264	$533,476,278	2.8
		208	$212,387,107	1.1
Other Research Grants	All	5,753	$1,510,024,350	7.9
	Career (K-grants)	3,516	$472,441,223	2.5
	U10	508	$444,429,728	2.3
	Other	1,729	$593,153,399	3.1
R&D Contracts	All	1,035	$1,416,940,438	7.4
Research Training	All	2,100	$555,817,043	2.9
Fellowships	All	2,731	$101,505,453	0.5
Other Awards	All	330	$170,007,677	0.9
Total Extramural		49,716	$19,074,464,796	100

NOTE: The numbers and amounts of awards in this table differ slightly from those in Table 2-1, because they come from different databases. The data for Table 2-1 come from the NIH Budget Office and are based on budget authority; the data in this table come from the NIH Office of Extramural Programs and are based on obligations. It is not possible to determine the percentage of the NIH budget going to R01s, say, compared with center grants, because the Budget Office data (which include the total amount of NIH funding) do not break out funding by activity code, e.g., P30 or R01, and the Office of Extramural Programs data (which break out funding by activity code) do not provide a comparable figure for the total NIH budget.

SOURCE: grants.nih.gov/grants/award/trends/fund9202.htm (for mechanisms) and grants.nih.gov/grants/award/research/rgmechact9802.htm (for activity codes).

1992, when R01s accounted for 43 percent and centers for 10.7 percent of extramural research funding (NIH, 1995).

Although the amounts of funding going to the various mechanisms can be compared, in practice, centers—and other modes of research supported by NIH—do not operate independently. Typically, the mechanisms are planned and administered as a portfolio of complementary ways to increase knowledge and ways to apply it. This fact is most apparent in the case of P30 core grants. Core grants do not fund research per se, but only provide an organizational setting and technical resources (through core services and facilities) for a group of investigators already funded by other grants. In most cases, centers are not permitted to apply for a center award unless they have a minimum number of funded investigators working on projects related to the center's focus of research. The intent of such center grants is to increase the productivity of R01 and other NIH-supported research both by providing opportunities for interactions and joint projects among investigators and by expanding their access to research services and tools that individual grants could not afford. NIH supports research as part of some center awards (namely, the P50s, P60s, and U54s), usually because the type of research (e.g., interdisciplinary, translational, and clinical) would not fare well in the RPG review process. But even in that type of research center, center members often have R01 and other grants. Centers are also often a location for training in interdisciplinary or translational research of physicians, postdoctoral students, and graduate students who are supported by other means, such as NIH training grants. The principal investigators of clinical research networks and groups are often members of centers, and the centers are usually part of the infrastructure for clinical trials.

Examination of recent invitations to submit proposals for center support (i.e., Requests for Applications [RFAs] and Program Announcements [PAs] published by NIH between 2001 and 2003) yielded the following synthesis of the major justifications offered for centers or center programs:

- Centers enable a stable, long-term institutional focus on a complex set of problems that cross disciplinary lines that is not likely to occur through R01s alone, because the multidisciplinary milieu of a center fosters scientific interactions and collaborations that can stimulate scientific creativity and speed new developments in an area of research more effectively than would be possible with individual investigators working in relative isolation.
- Centers can support translational, clinical, behavioral, and epidemiological research that has not typically fared well in the discovery-oriented system for peer review of investigator-initiated research proposals, thus hastening translation of fundamental knowledge into clinical advances and clinical advances into practice.

- By making expensive resources accessible, centers can enhance the quality, facilitate the productivity, and promote the cost-effectiveness of R01, P01, and other externally supported research projects, while encouraging interdisciplinary collaboration.
- Some center programs fund pilot research projects, which help investigators develop preliminary data to support innovative R01 applications, or support new investigators until they successfully compete for an R01 grant or other independent support.
- Designation as an NIH-supported research center confers distinction on the area of research and thus helps attract additional competitive research funding from private as well as public sources, facilitates fund raising, increases the interest and support of medical school leaders and colleagues, and supplies a valuable incentive in recruiting new faculty, staff, and trainees.
- Located in academic medical centers across the country, centers can be an important mechanism for facilitating the transfer of clinical research results into community practice by developing and then demonstrating the latest techniques. They can also develop and disseminate consistent definitions and standardized research methods, conduct demonstration projects, and conduct community and professional education and outreach.
- Supporting research centers is a means of building research capacity in institutions and regions that have not competed well for peer-reviewed grants from NIH or other funders of research. Broadening the distribution of research funding across the country is the purpose of a number of center programs, such as NCRR's Centers of Biomedical Research Excellence and Biomedical Research Infrastructure Network, Specialized Neuroscience Research Programs at Minority Institutions of the National Institute of Neurological Disorders and Stroke (NINDS), and the Cooperative Reproductive Science Research Centers at Minority Institutions of the National Institute of Child Health and Human Development (NICHD).
- A network of similar centers can combine their resources to ask questions that no one institution could address alone, and technology is making this easier. The most obvious case is that of large clinical trials, in which such a network can take advantage of a greatly expanded patient pool to conduct the trial faster and more efficiently than would be possible in any single site. Networks of centers are becoming more important in basic research as well, because researchers are trying to understand complex biological systems that require the participation of many kinds of expertise that previously have not interacted.
- Center awards are a way to build research infrastructure to respond to public health emergencies, as is being done with the rapid imple-

mentation of the National Institute of Allergy and Infectious Diseases' (NIAID's) Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research.

Chapter 5 describes some of the challenges to determining whether these laudatory goals are actually met. In addition, the center mechanism as a research strategy is not without critics, who argue that, as in any complex human endeavor, not all of these goals will be realized in every center. For example, long-term support may actually detract from a productive research program if substantial sums of money are committed to centers that are only moderately productive, money that might otherwise be available to fund traditional R01 grants and other externally conceived research that are peer reviewed individually for merit (NIAMS, 1997). Critics might also point out that, although core grants may enable a center to promote interactions among researchers from diverse disciplines, those researchers must already have individual, and commonly single-discipline, grants of their own, usually from the same institute funding the center, which may inhibit interaction.

A third point offered by critics stems from the initiation of center programs by NIH institutes rather than by the extramural scientific community. That is, the institutes issue an RFA or PA describing in some detail what they expect to see in the proposals for centers that are submitted. Many observers (e.g., Teitelbaum, 2003) attribute the success of NIH over the past four decades to its deliberate policy of relying on the judgment of the scientific community as a whole, through investigator-initiated proposals, to determine the scientific agenda and identify the areas in which progress is most likely. Table 2-1 and Figure 2-2, above, show that NIH continues to rely primarily on investigator-initiated research project grants (of which R01s are a large majority) to take advantage of the expertise and creativity of the nation's scientific community. Although funding for center awards has been growing steadily over the past decade, as Figure 2-2 shows, the share of the NIH budget devoted to center awards has been stable at between 8 and 9 percent.

Center grants and other institute-initiated programs also differ from most individual-investigator-initiated and program project grants in the way that proposals applications are solicited and evaluated, and that difference also can be a source of friction within the scientific community. NIH sets its research priorities through a complex process that incorporates both scientific opportunity and the health needs of the nation (NIH, 2001; IOM, 1998). To address both opportunity and need, evaluation of individual research proposals is conducted through a two-stage review process. In the first stage, investigator-initiated proposals are reviewed by appropriate panels of outside experts, called study sections, organized by NIH's Center for

Scientific Review (CSR). Study sections are established according to scientific disciplines or current research areas, and their members are recruited by CSR from among the active and productive researchers in the extramural biomedical research community. The objective of this initial peer review is to evaluate and rate the scientific and technical merit of the proposed research. Each proposal is assigned a priority score by the study section, and the scores, together with the written reviews and a summary of the section's discussion and recommendations, are transmitted to the appropriate institute for funding consideration. A second-stage review then is done by the institute's national advisory council (also an external group), the focus of which is importance to the institute's programmatic priorities, which, in turn, reflect the institute's view of the health needs of the nation, as well as research opportunities, within the institute's mission. Most applications for funding reviewed by CSR are initiated by the investigators or are responses to broad program announcements. The peer review process is highly competitive, and on average only about 30 percent of investigator-initiated proposals submitted are funded, most of them in strict order of scientific priority score.[3]

The review process for institute-initiated proposals (i.e., responses to RFAs, PARs, and PASs) is also designed to take into account both health needs and scientific opportunity through a two-step process, but the initial peer review is conducted by an institute-appointed group rather than a CSR study section.[4] The institute's initial review group is charged with considering the institute's program priorities as well as scientific opportunity and excellence. The RFAs and institute-reviewed PAs also contain requirements for an acceptable proposal that embody the institute's priorities. In cases in which the award will fund individual research projects as well as infrastructure, reviewers are generally asked to provide not only a recommendation on the proposal as a whole but also on the merit of each proposed project. As a result, the proposal could conceivably be partially funded, without funds for one or more of the proposed research projects. Some skeptics argue that sometimes a research proposal that would not have been funded if reviewed by a CSR study section is nevertheless funded as part of a larger

[3]Each institute has a procedure for funding some applications of high program relevance whose priority scores would otherwise put them below the funding cutoff point.

[4]A PAR is a PA (program announcement) in which the first-stage review is conducted by an institute peer review group rather than a CSR study section. A PAS is the same as a PAR except, like an RFA, a stated amount of funding is set aside. It should also be noted that some well-established center programs (e.g., Cancer Centers and Environmental Health Science Centers) do not employ solicitations. As with investigator-initiated grants, the institute posts a periodic submission date. Unlike with investigator-initiated grants, however, applicants for these center grants must follow rather detailed guidelines published by the institute.

proposal that includes mostly meritorious activities (NICHD, 1999; NIAMS, 1997). The success rate of proposals in the initial round of funding may be low, for example, when 10-12 applicants vie for, say, three center grants, but subsequent success rates for center applications are usually higher than for individual-investigator renewal applications.

The large size and diverse nature of many centers also make both proposals and performance more difficult to evaluate than individual grants (see Chapter 5), and the prestige that helps attract outside funding and new researchers can make them highly sought-after awards independent of any analysis of whether they are an appropriate tool at that time and place (Korn, 2003).

A further concern raised about centers is that the vertical integration expected to lead to increased interaction among basic, clinical and preventive, behavioral, and population-based research cited above may not always materialize. Evidence for this may be inferred from revisions in established programs directed at increasing this type of activity, e.g., the introduction of SPOREs to supplement NCI's cancer centers in 1992 and reorientation of NHLBI's 30-year-old SCOR (Specialized Centers of Research) Program in 2001, symbolized by renaming them SCCORs (Specialized Centers of Clinically Oriented Research).

Similarly, attempts to use a center program to attract new researchers to a disease or field may sometimes have the opposite effect. The few good scientists already working in the field have a strong advantage in the competition for the new centers, resulting in the centers program concentrating resources still further in a small cadre of scientists.[5]

The merits of these positions, or at least approaches to judging their merit, are examined in more detail in Chapter 5, which deals with how to evaluate center programs. Generally, however, the committee is of the opinion that center programs are a valuable addition to NIH's array of funding mechanisms and provide an important source of support for clinical research aimed at translating basic science discoveries into useful clinical products and practices.

ALTERNATIVE RESEARCH MODELS

NIH currently employs a number of alternative mechanisms besides centers to foster and support interdisciplinary research, translational research, collaborations among researchers in different places, and research resources. In addition, there are or could be alternatives within the center model itself.

[5]There is a discussion of this issue with reference to the establishment of centers of excellence in autism research in NIH, 1999.

One alternative is to fund research teams or groups without imposing a center structure. Traditionally, these enterprises have been smaller than centers tend to be, although a recent trend toward large research networks will be discussed below. The program project (P01) grant to support a small group of investigators conducting research with a common theme has a long history preceding centers (in fact, the first grants for centers, in the 1960s, were coded as P02 program projects). P01 funds support shared research facilities and services (cores) as well as the research projects.

More recent alternatives include Investigator-Initiated Interactive Research Project Grants (IRPGs), in which related R01 research project grants are submitted together, and "mini" core grants, in which R24 (or U24) research resource-related grants are used to encourage already-funded investigators to work together on a problem by providing resources not available where investigators are working separately. The National Institute of Mental Health (NIMH), for example, sponsored a PA inviting applications for IRPGs for research integrating the basic behavioral sciences and public mental health.[6] NIDDK recently funded R24 "mini" centers, called Digestive Diseases Research Development Centers, for investigators without access to P30 Digestive Disease Research Core Centers.[7] NIGMS and NIDDK have issued a PA inviting consortia of funded investigators from different disciplines who want to collaborate on a multidisciplinary research problem to apply for R24 grants. According to the PA, the purpose of the R24 "consortium grant mechanism" is to "allow the participating investigators to (1) attract and coordinate expertise in different disciplines and approaches and (2) facilitate access to specialized resources and equipment."[8] The National Eye Institute (NEI), NCI, and NICHD are other institutes using R24 grants in this way.[9]

Another approach is to use cooperative agreements, such as the U01, U10, or U19, to facilitate collaboration among a number of individual investigators or small research groups in different locations and also provide for a steering committee to set overall priorities for all participants. An example is NIDDK's Inflammatory Bowel Disease (IBD) Genetics Research Consortium, which consists of six "IBD genetics research centers" and a data coordinating center supported with U01 cooperative agreements.[10]

Some institutes promote interdisciplinary collaboration by providing supplements to RPGs to support such activities. The Division of Cancer

[6]"Integrating the Basic Behavioral Sciences and Public Mental Health," PA-00-078.
[7]RFA-DK-01-030.
[8] "Integrative and Collaborative Approaches to Research," PA-03-127.
[9]"Vision Research Infrastructure Development Grants," PAR-02-050; "Shared Resources for Scientists Not at NCI Funded Cancer Centers," RFA-CA-01-020.
[10]RFA-DK-02-011.

Biology at NCI, for example, does this through a program called Activities to Promote Research Collaborations.[11] Seven NIH institutes and two National Science Foundation divisions have sponsored a PA inviting applications for R01 grants to develop and support tools for collaborations that involve data sharing.[12]

In some types of clinical research (e.g., clinical trials), coordinated activities by multiple clinical centers are needed, rather than direct interactions between basic researchers and clinical investigators for translational research purposes. In these cases, NIH often uses cooperative agreements (e.g., U10, U01, and U19 awards) or contracts. NHLBI supports a series of clinical research networks to conduct clinical trials in, for example, resuscitation from cardiopulmonary arrest (U01), chronic obstructive pulmonary disease (U10), and asthma (U10).[13] In FY2002, U-series awards accounted for more than 9 percent of the NIH budget ($1.8 billion), compared with the $1.7 billion spent on center awards (not counting NCRR funding of research resource centers).

In recent years, it has become possible to conduct large-scale biomedical research efforts in certain areas of science, for example, genomics and proteomics, where complex problems must be tackled with large interdisciplinary teams or large-scale facilities and resources are needed, or both. One example of interactive research networks or teams is NIGMS's Large-Scale Collaborative Project Award, known as the "glue grant" program. This program is supporting large consortia of researchers working on complex biological phenomena such as cell signaling, cell migration, and the body's response to trauma and burn injuries. Although glue grant consortia are supported with U54 center grants, the local organizational entities are not really centers in the traditional sense. NCI is using U54 center grants to develop several networks of translational research teams, one to focus on molecular targets for cancer drug development, another on optical imaging.

In other cases, institutes are using a combination of grants to create an integrated research initiative. The National Institute on Alcohol Abuse and Alcoholism (NIAAA), for example, is creating consortia addressing various problems, for example, fetal alcohol spectrum disorders and alcoholism. The consortia consist of a set of integrated research projects, each funded by a U01 cooperative agreement; several core facilities, each funded by a U24 research resource-related cooperative agreement; and a consortium

[11] NOT-CA-03-035.

[12] PAR-03-134.

[13] "Clinical Research Consortium to Improve Resuscitation Outcomes," RFA-HL-04-001; "COPD Clinical Research Network," RFA-HL-03-002; "Asthma Clinical Research Network," RFA-HL-02-029.

coordinator.[14] NCI's Early Detection Research Network consists of 18 biomarker development laboratories, 3 biomarker reference laboratories, 9 clinical epidemiology and validation centers, and a data management and coordinating center, each funded with a U01 or R24 award and all governed by a steering committee consisting of the Principal Investigators and a representative of NCI.[15]

It should also be noted that the center model itself has not been static. It has been evolving from the concept of a problem-focused organizational structure that cuts across disciplinary department lines within a research institution to a concept of centers as a network involved in collaborative as well as center-specific research. The concept is that if the centers are networked to share information and conduct collaborative studies, they are more effective than when each center works on its own. The recent autism, muscular dystrophy, and rare diseases center programs have been structured so that, in addition to traditional within-center interdisciplinary and translational research activities, there is between-center collaboration coordinated by an overall steering committee. In some cases, the institute provides a separate research fund for multicenter collaborative research.

Another alternative has been to use existing centers rather than create new ones for a specific disease or other problem. Some emerging research opportunities or health emergencies are met by providing supplements to centers. In another case, centers for research on fragile X syndrome, the centers are being located at centers for research on mental retardation and will become, in effect, a component of the existing centers. These alternatives have the virtue of speed and ease of implementation and take advantage of the technical and administrative experience of mature research institutions.

NIH has also been experimenting with Web-based virtual laboratories, also called "collaboratories." NCRR has funded seven collaboratories through supplemental awards to some of its existing P41 biotechnology resource centers (NCRR, 2000, 2002). One of these, the Biomedical Informatics Research Network, is developing the network, data-storage, and software tools needed for geographically separated investigators conducting research involving neuroimaging to share and use large sets of data on brain images from the molecular scale to the whole brain.[16]

The committee discussed some additional alternatives. One would be to allow individual investigators to apply for support of center projects

[14] "Collaborative Initiative on Fetal Alcohol Spectrum Disorders," RFA-AA-03-002; "Integrative Neuroscience Initiative on Alcoholism," RFA-AA-01-002.

[15] See http://www.cancer.gov/edrn.

[16] http://birn.ncrr.nih.gov/birn/birn.

whose form and structure are designed by the applicant rather than specified in a PA, RFA, or institute guidelines. This could lead to centers organized differently or addressing problems differently (or different types of problems) than those solicited by NIH. It might encourage collaborative translation, clinical, and population projects that investigators believe are too risky or novel to submit to study sections more oriented toward basic science projects. Another would be to broaden initiatives to reduce health disparities to encourage partnerships between centers in research-intensive institutions and rural health facilities. NIAID's Alzheimer's Disease Centers, for example, are affiliated with satellite diagnostic and treatment clinics that recruit minority, rural, and other underserved patients to increase the diversity of study volunteers.

PROBLEMS WITH THE DATA ON CENTERS

The data reported in the previous sections probably include most centers funded by NIH and are therefore useful for aggregate analysis of trends, but there are some problems:

1. *Not all centers are funded by center awards.* A perusal of the institute websites, RFAs, and PAs issued by the institutes, and the Computer Retrieval of Information on Scientific Projects (CRISP), NIH's database of funded awards, revealed a number of projects called centers by NIH, but funded by awards not classified and counted as center grants. For example, during calendar year 2002, NIH issued 48 RFAs and PAs with the word "center" in the title. Of the 50 grant types offered in these RFAs and PAs,[17] 11 (22 percent) were coded as RPGs or other research grants rather than as center grants. Examples include NHLBI's Centers for Reducing Asthma Disparities, which are being funded through U01 cooperative research project agreements; NIAID's Autoimmunity Centers of Excellence, funded through U19 cooperative research program agreements; NIAID's Asthma and Allergic Diseases Research Centers, funded by P01 program project grants; and NICHD's Population Research Centers, which are being switched from P30 core grant support to R24 resource-related research project grants. NIAID's Biodefense Proteomics Centers will be funded by contracts. These anomalies may reflect in part the fact that early in the formulation of the NIH budget, the Office of Management and Budget and the Department of Health and Human Services provide NIH with guidance on the amount of funding NIH should request. That guidance is specified

[17]Several of the RFAs offered several types of awards, for example, a P50 center grant and a P20 planning grant.

by mechanism. This constrains the "centers line" in the budget, and new center initiatives might therefore be funded through other mechanisms, for example, U19 or P01 awards in the RPG line or U10 awards in the other research line.

2. *Not all entities supported by center awards are called centers although they function as centers*. NCI, for example, supports Interdisciplinary Research Teams for Molecular Target Assessment to develop methods for preclinical and clinical research to use in assessing the effects of interventions directed at specific molecular targets. They are funded by U54 specialized center cooperative agreements. NCI also has P50 centers called SPOREs. The NIH initiative in biomedical computing is National Programs of Excellence in Biomedical Computing (NPEBC). Although called programs, NPEBCs will function like centers and be supported by U54 center grants. "NPEBC will provide a formal framework through which scientific synergy can occur on a stable and continuing basis, and will provide: (a) an organizational structure specifically designed to facilitate intellectual cross-fertilization between seemingly disparate groups of investigators; (b) core facilities to support research activities; (c) developmental funds for feasibility testing of new projects; (d) career development opportunities for new and established investigators; and (e) a broad range of educational activities, from formal undergraduate and graduate programs to courses and seminars for students and researchers, visiting scientists program or other types of training, cross-training, or educational approaches."[18]

3. *A number of NIH programs without "centers" in their titles and not using awards with research center activity codes share some of the features of many programs that have centers in their titles and employ awards with research center activity codes*. These programs fund research entities referred to by names such as "programs," "networks," "consortia," "research units," or "clinical centers." In many cases, these entities serve primarily as nodes in a network of sites intended to facilitate clinical trials by increasing the pool of potential patient-subjects. Funding can be by N01 R&D contracts, P01 program project grants, U01 cooperative research project agreements, U10 cooperative clinical research agreements, or U24 cooperative resource-related research project agreements; local research as well as participation in multisite projects is encouraged and sometimes included in the requirements for funding; and training clinicians and junior investigators is sometimes specified. Examples include NHLBI's Programs of Excellence in Gene Therapy (U01), NIAID's Acute Infection and Early Disease Research Network (U01), NIAAA's Collaborative Initiative on Fetal Alcohol Spectrum Disorders Consortium (U01 and U24), NIMH's Re-

[18]PAR-00-102.

search Units on Pediatric Psychopharmacology (N01), NIAID Tropical Disease Research Units (P01), and NICHD's Cooperative Multicenter Maternal-Fetal Medicine Units Network (U10).

4. *Alternative means are used to achieve some of the goals of center grants*. NIH can and often does fund coordinated multi-investigator research through other types of support, although these are usually smaller scale and not necessarily interdisciplinary. These projects are not called centers and are usually not solicited by an RFA, as most center grants are. Alternatives to centers for supporting team research, including interdisciplinary and translational research, include P01 program project grants (intended to support multiple investigators conducting research with a common theme); R24 infrastructure development grants (used like small core grants); U01, U09, and U19 collaborative research projects; and IRPGs (coordinated submission of related R01 and R29 applications).

Several institutes (e.g., NIAID and NINDS) publish guidelines for multiproject applications, including P01s, P50s, and U19s, regarding them all as efforts with a central focus or theme in which collaboration and interaction among investigators are expected to result in a greater contribution to the program goals than if each investigator pursued his or her project separately.

5. *Some large-scale research questions are being investigated through multi-institutional networks or consortia rather than centers*. In recognition of the impact of networking on certain kinds of complex research questions that cannot be addressed by a single center, some recent center programs (e.g., Autism Research Centers of Excellence) are setting aside funds from the center awards to support collaborative activities among the centers. In addition, new organizational models for conducting coordinated research by large interdisciplinary teams are emerging. One example is NIGMS's glue grant program, which is supporting consortia investigating complex problems that benefit from the interaction among and coordinated effort of many kinds of scientists and types of research. NIGMS calls it "the next evolutionary stage of integrative biomedical science." The glue grant is used to fund the interactions among the numerous and far-flung researchers involved in an area of research such as cellular signaling and cell migration.[19] The glue grant program uses a center award—the U54 cooperative agreement—after an initial organizational phase using an RPG award—the U24 planning grant. Other examples are the cross-disciplinary networks that NINDS is forming of scientists interested in studying the neural mecha-

[19]The Alliance for Cellular Signaling (http://afcs.swmed.edu/), for example, involves some 50 researchers in 20 academic institutions and several biotechnology companies, although the Alliance will have specially designed laboratory facilities at a half-dozen institutions (http://www.nigms.nih.gov/news/releases/gluegrant_release.html).

nisms of cognition and other complex behaviors. These Multimodal Integration Research Networks in Cognitive Neuroscience are funded by R01 grants. NIAAA has funded several interdisciplinary consortia of researchers from multiple sites as part of its Integrative Neuroscience Initiative on Alcoholism. The consortia are supported by a coordinated set of U01 cooperative agreements and distributed core facilities funded by U24s, led by a consortium coordinator and steering committee representing the principle investigators and NIAAA staff.

One solution to the problems of identifying and tracking center programs is to look at what they are intended to do, regardless of what they are called or the funding mechanism used. That is, one can identify the distinctive attributes of existing center grants and attempt to sort and track them on that basis.

The NIH *Glossary of Terms* provides the following definition:[20]

> Center grants are awarded to institutions on behalf of program directors and groups of collaborating investigators. They provide support for long-term multidisciplinary programs of research and development.

A more detailed definition is that contained in the NIH document called *National Institutes of Health FY2001 Investments*:[21]

> Research Center grants are awarded to extramural research institutions to provide support for long-term multidisciplinary programs of medical research. They also support the development of research resources, aim to integrate basic research with applied research and transfer activities, and promote research in areas of clinical applications with an emphasis on intervention, including prototype development and refinement of products, techniques, processes, methods, and practices.

The first of these two definitions is not specific enough to be useful in the present context. The second is specific enough to reveal that center grants are intended to support several different types of activities. An analysis of RFAs and PAs issued over the past few years confirmed that centers and center programs vary greatly in size, purpose, and organization, reflecting in part differences among research areas, for example, in the state of the knowledge, the amount of infrastructure needed for cutting-edge research, and the nature and burden of the health problem addressed. However, the committee believes that center awards fall into three broad categories, based on the kind of activity they support.

[20] http://grants.nih.gov/grants/glossary.htm.
[21] http://www.nih.gov/news/BudgetFY2002/FY2001investments.htm#centers.

1. *Center Infrastructure* awards, or "core" grants, fund a center's director and core services, administrative and technical, to support a group of investigators whose research is funded by independently obtained research grants. The primary goal of center infrastructure awards is to facilitate the conduct of research on a particular disease or scientific issue by enabling interactions and collaborations among investigators and by eliminating duplication and increasing efficiency in the provision of common and often expensive research tools and services. P30 core grants are the prototype, although some center programs use other types of awards to support center infrastructure (e.g., R24 resource-related research project grants).

2. *Research Center* awards fund not only core services but research projects as well. In some cases, they may also support additional activities such as community education, screening and counseling programs, and educating medical and allied health professionals about state-of-the-art diagnostic, prevention, and treatment techniques. Typically designed to encourage multidisciplinary or clinical research not being addressed by investigator-initiated projects, this group of centers includes many of the disease-based centers that Congress has mandated in recent years—e.g., Centers of Excellence for Parkinson's disease, autism, and muscular dystrophy. P50 and P60 grants and U54 cooperative agreements are the prototypes for this category of awards, but some centers of excellence are funded with P30 core grants. Noncenter awards are also employed in some center programs—e.g., Autoimmunity Centers of Excellence (supported by U19 cooperative agreements) and Centers of Excellence for Research on Complementary and Alternative Medicine (supported by P01 program project grants).

3. *Research Resource Centers* develop and provide research resources and tools to any researcher in the nation. Many of these centers are supported by NCRR (e.g., nonhuman primate centers, mutant mouse and other animal resource centers, and islet cell resource centers), although more institutes are developing such resource centers (e.g., NHLBI's proteomic centers, NIAAA's mouse mutagenesis centers, and NIAID's microbial genome sequencing centers). NCRR awards to resource centers are classified as center awards (e.g., P40, P41, P51, U41, and U42). Resource centers established by other institutes are supported by a variety of noncenter award types, although NHGRI and NIGMS use the P41 biotechnology resource grant.

Owing to the ambiguities of NIH's award classification described previously, a precise estimate of how many center awards might fall into each of these categories is not possible, but a rough approximation might be:

- Center infrastructure (core) grants, 20-30 percent
- Research centers, 45-50 percent
- Research resource centers, 20-30 percent

Although the taxonomy developed by the committee identifies three categories of center awards, only the first two categories, those for center infrastructure and for research centers, are the primary subject of congressional interest and legislation. The third type of center, the research resource center, although not explicitly excluded from the charge to this committee, is not the type of center that led to the congressional language mandating this study. Accordingly, subsequent discussion of centers and center programs in this report will include only centers of the first two types listed above.

Both center infrastructure (core) and research center awards are intended to promote and support research organizations that conduct interdisciplinary research on a medical problem or condition, or on a set of health-related scientific questions, or both, that would not be done as effectively or at all by other modes of research. Many of these centers also have additional functions that are a prerequisite for an NIH center award, such as research training and career development, public outreach, and professional education.

Finding. NIH does not consistently apply either the term "center" or center award activity codes to centers. This inconsistency makes it difficult to describe accurately the extent of research funding devoted to support of centers or evaluate the relative effectiveness of center awards or how well center programs complement other NIH-funded activities.

Recommendation 1. NIH should adopt or develop a coherent classification system with functional criteria that should be uniformly applied across all institutes for the categorization of all NIH-funded centers. The three functional categories of centers offered above by the committee represent one possible system of classification. All activities that fit in one of the categories in the classification system adopted or developed by NIH should be identified as centers, regardless of the name of the program or mechanism of funding.

Consistent identification of center programs and allocation to uniform categories will benefit NIH in terms of more informed public debate and understanding, greater NIH accountability, and better program evaluation. At the same time, a broad classification system such as the one we offer (NIH can adopt, revise, or replace it with its own), which includes just three types of center programs, leaves enough flexibility within the categories to

design each center program in the most appropriate way to achieve its particular goals.

REFERENCES

IOM (Institute of Medicine). 1998. *Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health*. Washington, DC: National Academy Press.

Korn D. 2003. *Statement of the Association of American Medical Colleges to the IOM Committee on NIH Centers of Excellence*. Presentation to the IOM Committee on Centers of Excellence at NIH, Washington, DC.

NCRR (National Center for Research Resources). 2000. *NCRR Biomedical Collaboratories Workshop Report*. [Online]. Available: http://www.ncrr.nih.gov/biotech/btcollab wrkshprpt10-2000.pdf [accessed December 15, 2003].

NCRR. 2002. *Data and Collaboratories in the Biomedical Research Community*. [Online]. Available: http://www.ncrr.nih.gov/biotech/collabmtg2002.asp [accessed December 15, 2003].

NIAMS (National Institute of Arthritis and Musculoskeletal and Skin Diseases). 1997. *Executive Summary, Report to the Institute Director of the Centers Working Group II*. [Online]. Available: http://www.niams.nih.gov/ne/reports/sci_wrk/1997/cenrptfn.htm [accessed December 15, 2003].

NICHD (National Institute of Child Health and Human Development). 1999. "Report of the Demographic and Behavioral Sciences Branch Population Centers Review." [Online.] Available: http://www.nichd.nih.gov/about/cpr/dbs/pubs/report.pdf [accessed December 15, 2003].

NIH (National Institutes of Health). 1995. *NIH Extramural Trends, Fiscal Years 1985-1994*. Bethesda, MD: Division of Research Grants, NIH.

NIH. 1999. *Report of Integrative Issues Working Group*. Summary of workshop: Treatments for people with autism and other pervasive developmental disorders: Research perspectives. Bethesda, MD: NIH Autism Coordinating Committee. [Online]. Available: http://www.nimh.nih.gov/research/autismworkshop.cfm [accessed December 15, 2003].

NIH. 2001. *Setting Research Priorities at the National Institutes of Health*. Revised edition. [Online]. Available: http://www.nih.gov/about/researchpriorities.htm [accessed December 15, 2003].

OMB (Office of Management and Budget). 2003. *Historical Tables, Budget of the United States Government, Fiscal Year 2004*. Washington, DC: U.S. Government Printing Office.

Teitelbaum S. 2003. Statement to the IOM Committee on Centers of Excellence at NIH, Washington, DC.

U.S. DHHS (U.S. Department of Health and Human Services). 2003. *NIH (National Institutes of Health) FY2004 Congressional Budget Justification*. [Online]. Available: http://www.nih.gov/news/budgetfy2004/fy2004presidentsbudget.pdf [accessed December 15, 2003].

3

Initiation and Management of Center Programs

This chapter examines the current procedures for initiating new programs of extramural research support at the National Institutes of Health (NIH), including new center programs, and how NIH manages center programs after they have been launched. The chapter also contains recommended changes that would make the decision-making process more explicit and systematic, which in turn would make the process more understandable to NIH's attentive publics. These changes in process, along with more explicit and uniform criteria—as recommended in the next chapter—will help ensure that the center mechanism is used when it is most appropriate.

The decision to create a new center program must be well justified. Centers should promise to have a substantial positive impact in their area of research because they represent a relatively large and longer-term investment than most other types of NIH awards to support research, they are more complex to manage in terms of peer review of proposals and staff oversight than a program of individual-investigator grants, and because of their size, they are more visible at the local level and can be politically difficult to terminate if the original purpose of the program is achieved or becomes obsolete.

Centers are established to achieve specific goals in a particular NIH initiative or program, for example, to help solve a specific problem such as cancer, AIDS, disabilities of the elderly, or bioterrorism; accelerate progress in a new field such as genomics and proteomics; or develop a new scientific technique such as bioinformatics and molecular imaging. This means that

the design of the program must be carefully considered in the initiation phase. A number of important decisions must be made to ensure that the stated goals are realistic and can be met. These decisions include determining the number of centers, type of award, size of award, eligible institutions, program components to be required, institutional commitments expected, relationships with other NIH-supported activities, reporting elements needed for evaluation of the program as a whole as well as of individual centers, and program location and structure at NIH. Careful initial program design, such as developing procedures and criteria for peer review, reporting of results, and program evaluation, also simplifies management of the program once it is launched.

INITIATION OF CENTER PROGRAMS

The initial decision to establish a center program is a very important step in program planning at NIH. That is the point at which the program must be justified in the context of the other mechanisms that NIH has to achieve its goals concerning a particular disease or scientific opportunity.

The series of events culminating in the establishment of a new program of centers is highly varied and complex. There are many sources of ideas for new center programs and multiple ways such ideas are recommended to NIH, but before a proposal to establish centers can be implemented, it must go through the process of planning and budgeting that NIH and its institutes use to develop and decide on new program initiatives. Proposals for new center programs are also part of a broader set of planning and budgeting activities resulting in NIH's annual budget request. After the appropriations are made by Congress and approved by the President, if funding permits, the new program is established and the process of soliciting applications for center awards begins.

The varied origins of center programs are described first, followed by a description of the planning and budgeting process through which center and other programs are adopted.

ORIGINS

Proposals to establish centers may originate from any of a number of sources. An analysis of 21 recent center programs established at NIH (based on all Requests for Applications [RFAs] and Program Announcements [PAs] issued for the first or second time between the beginning of 2002 and the end of February 2003) shows that proposals for new center programs come from many places and follow a variety of routes. The sources of origin of these 21 center programs (listed in Table 3-1) include:

- NIH external advisory groups
- NIH institute strategic plans
- Scientific workshops supported by NIH
- NIH program staff
- Federal interagency coordinating group
- Advocacy organizations
- Congress
- National commission
- Institute of Medicine report

NIH External Advisory Groups

External advisory groups to NIH have suggested the establishment of centers in a number of cases. For example, a special emphasis panel convened by the NIH Office of Rare Diseases in 1997 was instrumental in establishing the Rare Diseases Clinical Research Centers network, as mentioned above in Chapter 1. In 1995, a working group appointed by NIH on the state of science in autism recommended "creation of centers for long-term engagement in the field of biological clinical research" on autism (NICHD, 1995), and Congress mandated five such centers in 2001. In 1999, the report of the Task Force on the NIH Women's Health Research Agenda for the 21st Century recommended encouraging multidisciplinary work on women's health by, among other means, creating "core centers to encourage close cooperation, communication, and collaboration among investigators with similar interests," and the report is cited in the RFA for Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health issued in 2001.[1]

External advisory groups also may be involved in the implementation of center programs after they have been initiated elsewhere or mandated by Congress. NIH relies on such advisory groups to advise on the purpose and structure of center programs and to suggest appropriate research topics. In some cases, the advisory group is asked to develop an overall research plan in an area that addresses all possible mechanisms, not just centers. An example would be the NIH Muscular Dystrophy Research Task Force, which held its first meeting in May 2002 and identified the role, functions, and structure of centers for muscular dystrophy research. They suggested additional mechanisms to increase the training of clinical and basic science

[1]The report, *Agenda for Research on Women's Health for the 21st Century*, is at http://www4.od.nih.gov/orwh/report.pdf. An Institute of Medicine report, *Exploring the Biological Contributions to Health: Does Sex Matter?* (2001), also contributed to the initiation of this center program (http://www4.od.nih.gov/orwh/02SpecialProjects.pdf).

researchers; encourage cooperative research, innovative research, and translational research; establish repositories of tissue, DNA, cell lines, and other shared materials; create forums for the exchange of information and data; develop animal models; and develop informatics (NIAMS, 2002).

NIH Institute Strategic Plans

A number of center programs have emerged from the National Cancer Institute's (NCI) strategic planning process in recent years. In 1998 NCI changed the process for producing its annual "bypass" budget into a strategic planning exercise involving a large number of people inside and external to NCI.[2] In 2002, an RFA to establish a network of research teams conducting translational research in optical imaging was included among the "Extraordinary Opportunities" in imaging identified in the bypass budget (several workshops held by NIH had also identified opportunities in optical imaging). The Centers of Excellence in Cancer Communications Research program was part of another strategic plan initiative to take advantage of extraordinary opportunities in cancer communications. Earlier center programs developed in the bypass budget strategic planning process include the In Vivo Cellular and Molecular Imaging Centers and Transdisciplinary Tobacco Use Research Centers.

In 2002 the National Institute of Allergy and Infectious Diseases (NIAID) assembled a blue-ribbon panel on bioterrorism to develop a strategic plan for biodefense research. The plan calls for the development of 6 to 12 Regional Centers of Excellence for Bioterrorism and Emerging Diseases Research (NIAID, 2002). In August 2002 NIAID released an RFA inviting applications for up to four Regional Centers of Excellence for Bioterrorism and Emerging Infectious Diseases Research in fiscal year (FY) 2003.

Scientific Workshops

Several recent center programs trace their origins to scientific workshops sponsored by NIH. In some cases, the consensus report of a workshop had explicitly recommended centers. Centers with human embryonic stem cell core facilities, for example, were suggested by a workshop on the basic biology of mammalian stem cells held by the National Institute of

[2]The War on Cancer Act of 1971 authorized NCI to submit its annual budget directly to the President. It is called the bypass budget because it bypasses the Department of Health and Human Services and the Office of Management and Budget (NCI also submits a regular budget request).

TABLE 3-1 Origins and Intended Purposes of Recent Center Programs

Program	Origins	
	Proposed by Outside Group(s)	Mandated by Congress
Rare Disease Clinical Research Network (U19)	X	X
Excellence in Partnerships for Community Outreach, Research on Disparities in Health and Training (Project EXPORT) (P60/P20/R24)		X
Comprehensive Centers on Health Disparities (U54)		
Transdisciplinary Prevention Research Centers (P50/P20)		
Centers of Excellence in Chemical Methodologies and Library Development (P50)	X	
Centers of Excellence for Research on Complementary and Alternative Medicine (P01/U19/R21)	X	
Research Core Centers for Advanced Neuroinformatics Research (P30)	X	
Breast Cancer and the Environment Research Centers (U01)	X	
Muscular Dystrophy Cooperative Research Centers (U54/R21)	X	X
Exploratory Center Grants for Human Embryonic Stem Cell Research (P20)	X	
Regional Centers of Excellence for Biodefense and Emerging Infections (U54/U56)	X	
Cooperative Centers for Translational Research on Human Immunology and Biodefense (U19/R21)	X	
Network for Translational Research: Optical Imaging (U54)	X	
Centers of Excellence in Complex Biomedical Systems Research (P50)	X	
Autoimmunity Centers of Excellence (U19)		X

	Intended Purpose			
PriorNIH Initiative(s)	Interdisciplinary	Translational	Training	Shared Resources
X	X		X	
	X		X	X
	X		X	
	X	X	X	X
	X			X
X	X		X	X
X	X	X	X	X
X	X	X		
X	X	X	X	X
	X		X	X
	X	X	X	X
	X	X	X	X
	X	X	X	X
X	X		X	X
X	X	X	X	X

Continued

TABLE 3-1 Continued

Program	Origins: Proposed by Outside Group(s)	Origins: Mandated by Congress
Cooperative Reproductive Science Research Centers at Minority Institutions (U54)	X	
Centers for Population Health and Health Disparities (P50)	X	
Centers of Excellence in Cancer Communications Research (P50)	X	
Autism Research Centers for Excellence (U54/R21)	X	X
Institutional Core Grants to Support Neuroscience Research (P30)		
Fragile X Research Centers (P30)		X

NOTE: External idea means that centers were recommended by an external advisory body or other outside group. Prior initiatives are earlier PAs, RFAs, or Requests for Proposals (RFPs) inviting applications for research project grants, program project grants, or other noncenter research mechanisms to address a problem or condition.

General Medical Sciences (NIGMS) in 2002 (NIGMS, 2002). Another NIGMS workshop, held in 2000, concluded that improvements in chemical methodology for the development of chemical diversity libraries were needed for biological research and that a "center-like" mechanism would be an effective means of encouraging collaborative research between chemists and biologists (NIGMS, 2000). The result was RFAs for Centers of Excellence in Chemical and Library Development through which four centers were funded in 2002 and 2003. In other instances, NIH staff members have determined that centers would be an appropriate response to the research opportunities identified in a workshop, if workshop participants had not addressed the question of mechanisms (see below).

NIH Program Staff

Transdisciplinary Prevention Research Centers is an internally generated program proposed in 2001 by a staff committee that had been charged by the director of the National Institute of Drug Abuse with identifying nonincremental initiatives. In some cases, after an external advisory committee has identified research needs and opportunities but not specific

	Intended Purpose			
PriorNIH Initiative(s)	Interdisciplinary	Translational	Training	Shared Resources
	X	X	X	X
	X	X		X
	X	X	X	X
X	X	X		X
	X			X
	X		X	X

SOURCE: Lists of RFAs and PAs by year and week in online NIH Guide for Grants and Contracts. Available at http://grants.nih.gov/grants/guide/index.html. The table includes all center programs with the first or second RFA or PA published between January 1, 2002, and February 27, 2003.

mechanisms, staff may suggest that centers and perhaps other mechanisms be established to carry out the research agenda. For example, a 1997 workshop convened by NIGMS on approaches to the study of complex biological processes concluded that the institute should launch an initiative to support cross-disciplinary and collaborative research projects aimed at understanding fundamental aspects of complex biological phenomena, such as questions of complex multigene and gene product interactions, membrane signal transduction and responses to subtle environmental factors, and differentiation and development in model systems. Workshop participants did not recommend centers or any other specific mechanisms, but they called for ways to encourage physicists, mathematicians, engineers, computer scientists, and other experts with quantitative skills to collaborate with biomedical scientists, for programs to increase the number of biomedical scientists with the requisite quantitative and computational expertise, and for support of research resources, such as new software and databases, and expensive instrumentation (NIGMS, 1998). NIGMS undertook a number of initiatives to promote and support research on complex biological systems in 1998 and 1999 (e.g., RFAs inviting applications for R01 and P01 grants for quantitative approaches to the analysis of complex

biological systems and R21 grants for integrative and collaborative approaches to research). The number of applications and awards in response to the initiatives was disappointing, however, and staff recommended a program of centers to encourage interdisciplinary research and training in computational biology and bioinformatics. In 2001 NIGMS issued an RFA for Centers of Excellence in Complex Biomedical Systems Research, which was reissued in 2002, and four centers have been funded.[3]

Federal Interagency Coordinating Group

In 2002 a federal interagency coordinating committee (FICC), chaired by the director of the National Institute of Mental Health (NIMH) and including representatives from 16 agencies, initiated Research Core Centers for Advanced Neuroinformatics Research with a PAR.[4] The FICC was appointed by the Secretary of Health and Human Services to administer the Human Brain Project. The project has been implemented in phases, beginning with Phase I feasibility studies in 1993, followed by Phase II development and testing in 1999. Phases I and II used R01, P01, and P20 grants as mechanisms of research and infrastructure support. Phase III, the distribution of neuroinformatics tools to the scientific community, will include P30 core centers.

Advocacy Organizations

Many voluntary health organizations representing patients and their families lobby for larger NIH budgets in general and more funding for their disease or condition in particular. Sometimes, they advocate the creation of research centers. In some cases, an institute may agree that centers would be a useful mechanism to add to a research program and proceed to initiate a center program (the NIH planning and budgeting process is described in the next section of this chapter). In other cases, the institute may decide that centers would not be the best way—at least at that time—to make progress against a disease but might propose other initiatives, such as an RFA inviting investigators to apply for funding set aside for research project or program project grants, establishment of a network of clinical trial sites, and/or for supplements to existing grants. If the institute does not create a

[3]NIGMS also funded three P20 planning grants in 2002 to help promising research groups develop centers and apply for full center funding in response to the second RFA.

[4]A PAR is a Program Announcement in which applications are reviewed by an initial peer review group appointed by the originating institute rather than reviewed by a study section under the Center for Scientific Review.

center program, advocates may ask Congress to urge or require NIH to establish such centers, a situation discussed in the next section.

Advocacy groups pushed for several recent center programs, including Autism Research Centers of Excellence, Fragile X Research Centers; Muscular Dystrophy Cooperative Research Centers, Breast Cancer and the Environment Research Centers, and centers of excellence for research on rare diseases (Rare Diseases Clinical Research Network). A representative of the National Fragile X Foundation told Congress that curing fragile X syndrome requires interdisciplinary research and cooperative clinical trials, which centers could provide. "Collaborative efforts thrive in centers that are specifically designed and funded for such interactions. Thus far, individual grants in the field of fragile X have not led to treatment research" (Hagerman, 1999). Muscular dystrophy groups testified that centers provide an environment in which a critical mass of researchers could be assembled and that centers would promote rapid translation of research into treatments (U.S. Congress, 2001c). Advocates of autism centers presented the same rationale, and the language mandating muscular dystrophy centers in the muscular dystrophy bill of 2001 was the same as that mandating autism centers in the Children's Health Act of 2000. A representative of the National Organization for Rare Disorders (NORD) asked Congress "to consider the creation of four regional extramural diagnostic and research centers to expand patient outreach activities and facilitate the development of postdoctoral training fellowships," because "rare disease patients are particularly impacted by the cost of diagnosis, treatment, and ancillary support services that can reduce a family to poverty, and because patients must often travel long distances to academic hospitals to see the few specialists who work on their particular disease" (Dorman, 2001).

Congress

The appropriations committees often urge the NIH director or an institute director to consider using centers in appropriations report language, and periodically the authorizing committees mandate the establishment of a centers program by amending the Public Health Service Act. Congressional action on centers generally results from lobbying by advocacy organizations, although some members also take a personal interest in a particular disease.

The annual appropriations laws rarely include more than the total budget amount approved for each institute, but the appropriations committees can influence NIH decision making through the reports that accompany the bills. Report language does not have the force of law, and usually it "urges" or "encourages" rather than mandates NIH to create centers. NIH, however, tries to comply with report language as much as possible.

The reports with the FY2002 appropriation bills, for example, contained a number of items about centers, both existing and proposed. The House report (U.S. Congress, 2001a) included the following items:

> The Committee also encourages NCI to fully fund the four ovarian cancer SPOREs [Specialized Programs of Research Excellence] and accelerate research in this area through all available mechanisms, as appropriate, including the establishment of additional ovarian cancer SPOREs.
>
> NIDDK [National Institute of Diabetes and Digestive and Kidney Diseases] is also urged to enhance research in such areas as basic bladder disease, pediatric urology, and urinary tract infection through all available mechanisms, as appropriate, including establishing centers of excellence…The Committee requests that the Director of the Institute be prepared to report on the progress in this area at the fiscal year 2003 appropriations hearing.
>
> The Committee also urges ORWH [Office of Research on Women's Health] to enhance research on multisystemic diseases in women through all available mechanisms, as appropriate, including the establishment of interdisciplinary research centers. The Director [of NIH] should be prepared to provide a progress report at the fiscal year 2003 appropriations hearing.

The Senate report (U.S. Congress, 2001b) included these items:

> The Committee encourages NCI to fund at least three Specialized Programs of Research Excellence in Brain Tumors grants in the upcoming fiscal year, with particular emphasis on those proposals which include both basic research and clinical treatment applications.
>
> The Committee strongly urges the formation of prostatitis research centers under the direction of infectious disease specialists as separate and distinct entities from the urological centers.
>
> The Committee is also aware of the significant progress made at the George M. O'Brien Kidney and Urology Research Centers of the NIDDK. The Committee urges continued and increased funding for their activities. In addition, the Committee encourages the creation of two new urologic centers, both of which should have a clinical component and a research training component.
>
> The Committee further strongly urges the NIEHS [National Institute of Environmental Health Sciences] to establish centers to conduct multidisciplinary and multi-institution research on environmental factors that may be related to breast cancer.

NIH responses to such language in congressional reports have included issuance of RFAs and PAs for Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health (December 2001), a Chronic

Prostatitis Collaborative Research Network (September 2002), and Breast Cancer and the Environment Research Centers (November 2002).

The House and Senate authorizing committees may also pass authorization bills that establish center programs. The War on Cancer Act of 1971, which created the comprehensive cancer centers, was the first law to mandate a center program in law. The most recent center programs that have been mandated by law have been for Parkinson's disease (1998), autism (2000), fragile X syndrome (2000), muscular dystrophy (2001), and rare diseases (2002). These are usually cases in which NIH believes that centers are not the best way to stimulate progress in the field, but there is strong support for centers by advocacy groups, or they have been recommended by a blue-ribbon panel, or both, and Congress decides to mandate them despite NIH's judgment. The statement of the NIH director at a congressional hearing opposing the establishment of centers for research on Parkinson's disease was quoted in Chapter 1. In another case, a national commission proposed specialized centers for research on rare diseases in 1989 (see below). In 2001 an NIH special emphasis panel convened at the request of the Senate Appropriations Committee recommended "regional centers of excellence for rare diseases research and training." In response, Senator Kennedy introduced the Rare Diseases Act "to greatly enhance the prospects for developing new treatments and diagnostics, and even cures for literally thousands of rare diseases and disorders (Kennedy, 2001)." NORD (which had already asked the Senate Appropriations Committee to create four centers) and other organizations representing specific rare diseases lobbied for the bill, which was passed in October 2002. The act authorized the NIH director to award cooperative agreements or grants for rare disease regional centers of excellence.

The degree of specificity of a congressional mandate varies, and Congress, at the request of NIH, has reduced the statutory requirements in some cases. For example, a provision to create a specific number of centers for muscular dystrophy research ("no less than five") was dropped as the bill was being considered by the Senate appropriations subcommittee, giving NIH flexibility if there were fewer than five meritorious applications. NIH was permitted to establish the mandated fragile X centers within existing centers for mental retardation research. In other cases, NIH has not had to establish the centers immediately, but over several years, to give applicants more time to lay the groundwork for a strong center proposal.[5]

In other instances of congressional interest, NIH responds before a possible congressional mandate is enacted. For example, the Breast Cancer and the Environmental Research Act of 2001 would have required the NIEHS director to make grants for "not more than eight Breast Cancer and

[5]NIH often assists in this process by awarding one- or two-year planning grants.

Environmental Research Centers of Excellence."[6] The House and Senate bills, introduced in May 2001, had 193 and 41 cosponsors, respectively, and were supported by the National Breast Cancer Coalition. The Senate report accompanying the FY2002 appropriations strongly urged NIEHS to establish centers "to conduct multidisciplinary and multi-institution research on environmental facts that may be related to breast cancer" (U.S. Congress, 2001b). NIEHS's Division of Extramural Research and Training included the topics in the concepts considered at its annual science retreat, and a concept paper for an RFA was reviewed at the February 2002 meeting of the NIEHS national advisory council. The RFA for Breast Cancer and the Environment Research Centers was released in November 2002, inviting applications for centers working cooperatively as a national network.[7]

Voluntary responses by NIH do not always satisfy Congress and the advocates. In response to strong interest in autism research and recommendations of a 1995 NIH conference on autism convened at the request of Congress, the National Institute of Child Health and Human Development established a network of 10 program project grants called Collaborative Programs of Excellence in Autism (CPEA) in 1997. Despite the existence of CPEA and several other autism initiatives, however, Congress included a provision for not less than five Centers of Excellence for Autism Research in the Children's Health Act of 2000 (two centers were funded in September 2002 and six more in May 2003). In another case, even though NIH indicated in its FY2002 congressional budget submission that it planned to establish four centers for research on rare diseases, Congress subsequently mandated such centers by statute.

National Commission

In 1989 a national commission recommended that specialized centers be established to train researchers, develop diagnostics, and conduct clinical trials on diseases too rare to be targets of the pharmaceutical industry (National Commission on Orphan Diseases, 1989).[8] An important goal of

[6]107th Congress, H.R. 1723/S. 830, introduced May 3, 2001 (http://olpa.od.nih.gov/legislation/107/pendinglegislation/breastcancerrev.asp).

[7]NIEHS and NCI co-funded four Breast Cancer and the Environment Research Centers on October 14, 2003.

[8]The National Commission on Orphan Diseases was established by Congress in 1985 to assess the activities of NIH, Food and Drug Administration, and other agencies in connection with basic, applied, and clinical research and dissemination of research knowledge on the prevention, diagnosis, and treatment of rare diseases (Public Law 99-91, "Orphan Drug Act Amendments"). The 20 members of the commission were appointed by the Secretary of Health and Human Services.

the proposed center program was to attract patients scattered around the nation in sufficient numbers to conduct clinical trials. Earlier examples include the National Commission on Diabetes, which recommended creation of the Diabetes Research and Training Centers program in 1975, and the National Commission on Arthritis and Related Musculoskeletal Diseases, which called for the creation of Multipurpose Arthritis Centers in 1976 (now being replaced by Multidisciplinary Clinical Research Centers for Arthritis and Musculoskeletal and Skin Diseases).

Institute of Medicine Reports

Research Core Centers for Advanced Neuroinformatics Research were initiated by the federal interagency coordinating committee for the Human Brain Project, but the Human Brain Project, including the phased approach adopted by the FICC, was initially proposed in a 1991 report of the Institute of Medicine, *Mapping the Brain and Its Functions: Integrating Enabling Technologies into Neuroscience Research* (IOM, 1991).

Other Sources

Some earlier center programs have come from ideas proposed by additional sources. The Centers for Children's Environmental Health and Disease Prevention Research program was initiated by NIEHS and the Environmental Protection Agency in response to the 1997 Executive Order of the President, "Protection of Children from Environmental Health Risks and Safety Risks." Other centers have resulted from interactions with other agencies, such as the Centers for Oceans and Human Health, co-funded by NIH and the National Science Foundation, and Native American Research Centers for Health, co-funded by NIGMS and the Indian Health Service.

Multiple Sources

In many cases, center programs have originated from interactions among several parties, and it is impossible to identify a single originator. In some cases, for example, NIH program staff members organized a workshop on a topic of interest to the scientific community. The workshop identified promising research opportunities and needs and discussed centers as one way to foster interdisciplinary research or to develop and provide enabling technologies. NIH staff members then proposed initiatives, including the establishment of centers if there was a perceived need for expensive specialized research facilities or equipment that could be shared or for the collaboration of experts in different fields who did not currently interact. In other cases, organizations advocating for patients with specific diseases ask the congressional appropriations subcommittees to have NIH do more for

their patients. One or both committees then might request that NIH hold a scientific workshop or develop a research plan for attacking the disease. The workshop or the plan identifies research opportunities and needs and may suggest specific initiatives, such as the creation of centers, as a useful means of making progress, or NIH may develop an implementation plan that calls for centers.

An example is the centers of excellence for research on rare diseases program, classified above as congressionally mandated (which it was), but tracing its origins to many sources. NORD was founded in 1983 as a byproduct of the effort by advocacy groups to pass the Orphan Drug Act of 1983. NORD helped push for the appointment of the National Commission on Orphan Diseases by Congress in 1989, which recommended specialized centers to train researchers, develop diagnostics, and conduct clinical trials. Each year, NORD and its constituent groups asked NIH and Congress to increase research on rare diseases. In 1996 the Senate Appropriations Committee requested a report on the coordination of rare diseases research. In response, NIH convened the special emphasis panel to develop recommendations for stimulating research on rare diseases and conditions, using research resources, coordinating rare diseases research and development activities, and identifying emerging opportunities in rare diseases research. The 23 panel members came from academia, industry, and NORD. The panel's 1999 report contained 19 recommendations, one of them that "NIH should support the establishment of Specialized Research and Diagnostic Centers of Excellence for Rare Diseases to stimulate research and aid in the diagnosis of rare diseases" (NIH, 1999). The panel suggested starting with 10 centers and adding 10 a year until there were 40 centers. In the FY2002 congressional justification budget released in early 2001, NIH said it would develop four Regional Centers of Excellence for Research on Rare Diseases, to "provide expert consultation from researchers for patients with life-threatening rare diseases; stimulate research on diagnostic approaches, technology, and follow-up of clinical studies on rare disease treatments; and provide postdoctoral fellows with scientific exposure to rare diseases, syndromes, and conditions" (NIH, 2001a). At the Senate hearing on FY2002 NIH appropriations, NORD called for the creation of four centers. Legislation authorizing centers was introduced later in 2001 as "the fruition of a long, deliberative process involving both the Congress and the NIH." The Rare Diseases Act of 2002 was passed in the next session of Congress. In February 2003 the RFA for the rare diseases center program was released, inviting applications for up to four clinical research centers and a data coordinating center to form a Rare Diseases Clinical Research Network.[9]

[9]NIH funded seven Rare Diseases Clinical Research Centers and a Data and Technology Coordinating Center on November 3, 2003.

NIH PROGRAM PLANNING PROCESS

Proposals of new initiatives such as center programs are considered in NIH's annual planning and budgeting process. That process is elaborate and open, with many steps involving input from external advisory groups, meetings with voluntary health associations and patient advocacy groups, strategic planning exercises, and review by an institute's national advisory council (NIH, 2001b). It is a very decentralized process that varies from institute to institute, and it is generally informal in terms of procedures and criteria for adopting new programs.

The annual federal budget process is the principal driver of the program planning and priority-setting process, resulting in decisions about the existence of and amount of funding for programs. Although the federal budget process is an executive function, NIH and its institutes look beyond internal staff initiatives to the views and recommendations of constituency groups of many kinds, the Administration, and Congress. The institutes engage in multiyear long-range strategic planning, periodic program reviews, and research agenda-setting exercises, all involving outside advice from standing and ad hoc advisory groups. NIH-wide planning and program collaboration and coordination are less well developed, although the increasing focus of research on complex biological phenomena that cross institute boundaries is resulting in more multi-institute programs (including center programs) and more NIH director-level advisory mechanisms. Ultimately, all proposals to establish new programs of centers compete with other new and existing programs for funding in the budget process, unless NIH has been directed to establish centers from above by the Department of Health and Human Services (DHHS), White House, or, most often, by Congress. If centers are mandated, NIH must establish them regardless of what their priority would have been within the NIH planning system, and if Congress specifies the amount of funding for a center program in the appropriations process, NIH must accommodate that amount in its budget regardless of its impact on other programs.

Appendix D contains a more detailed description of program planning and budgeting at NIH, with many examples involving center program initiatives.

Strategic Planning

Each NIH institute prepares five-year strategic plans with input from nonfederal scientists and nonscientists representing health groups. They differ from institute to institute in their scope and level of detail, although each identifies four or five goals and areas of promising research in which advances would help achieve each goal. Some also identify specific programs or mechanisms as possible program initiatives, and new center pro-

grams have resulted from strategic plans, for example, Centers of Excellence for Bioterrorism and Emerging Diseases Research.

Only a few strategic plans contained explicit treatments of the relative advantages of alternative funding mechanisms. The plans that weighed mechanisms as alternative means for achieving goals tended to be from institutes that already had been conducting strategic planning before it was mandated by the NIH director in 1998 (e.g., NCI and National Eye Institute [NEI]) or had rather formal planning processes (e.g., NIAID and NIDDK). Strategic planning at NIH is still new for most institutes and not yet strongly linked to the annual planning and budgeting process.

Annual Program Planning and Budgeting Process

Each institute has its own process for program planning and decision making, culminating in a budget request to the NIH director each spring. In each institute, the process is complex and includes input from a number of outside sources, including advisory bodies, scientific workshops and conferences, and professional and consumer health groups. The institute directors then work with the NIH director to make final decisions on what goes forward to DHHS each June.

Generally speaking, in addition to long-range strategic planning, institutes sponsor workshops to identify research needs and opportunities, engage in periodic program reviews, and meet with professional and citizen groups on a continuous basis. At some point, often in a staff retreat held during the summer or early fall, potential initiatives are identified and discussed. After further work, the initiatives are reviewed by the institute's national advisory council. The institute director then decides which initiatives to include in the institute's budget request (and which to pare or eliminate if the Office of Management and Budget [OMB] or Congress allows less funding than requested). At the next national advisory council meeting, concepts for new initiatives that will be implemented through RFAs, PAs, or RFPs are presented and discussed and perhaps turned down or returned for further work.

The NIH director works with the institutes to prepare the NIH-wide budget request and has final approval authority on the distribution of funds among mechanisms and institutes. At all stages of the budget, the amount of funding for Research Project Grants (RPGs), especially for new and competing renewal grants, is scrutinized closely, relative to the amounts for other mechanisms, such as centers and contracts. And throughout the process, the institute directors, division directors, and program staff interact with scientific and lay stakeholders, consider the results of scientific workshops, blue-ribbon panels, and program reviews, and respond to the priorities of the NIH director, DHHS, and Congress.

In recent years, NIH directors have increasingly used their budget authority to stimulate trans-NIH programs. Harold Varmus, when he was director of NIH, used the director's discretionary fund and authority to transfer up to 1 percent of an institute's budget to address NIH-wide priorities, for example, expansion of the mouse genetic sequencing center program. The current NIH director, Elias Zerhouni, has requested a larger discretionary fund ($35 million instead of $10 million) to implement initiatives addressing needs in areas such as bioinformatics, molecular libraries, systems biology, and clinical research that individual NIH institutes cannot easily provide.

The NIH director then interacts with DHHS as it reviews NIH's preliminary budget estimate. In August DHHS gives NIH a budget "mark" for submission to OMB. The main submission is the NIH mechanism table. After OMB gives NIH its budget mark in late November, the NIH director consults with the institute directors and departments to decide whether to appeal the OMB mark to the President. After the final budget amount for NIH is settled, NIH revises the budget to fit and detailed budgets are submitted to Congress for each of the 24 grant-making institutes and centers, Office of the Director, and Buildings and Facilities.

Congressional Budget and Authorization Process

The appropriations process may have its own impact on new programs. The appropriations subcommittees for NIH put little detail into law, usually just the total for each appropriation amount for each institute. Instead, they use the reports that accompany bills to influence NIH, up to and including mandatory directives, for example, to establish a centers program. When the budget becomes law, there are three reports—the House report, Senate report, and report of the conference committee negotiated between the House and Senate on the final appropriations bill—and any directives in the report of one committee remain in effect unless contradicted in the report of the other subcommittee or the conference committee report. Although report language does not have the force of law, NIH tries to comply with directives, because it has to appear before the appropriations subcommittees every year for funding.

In recent years, the appropriations subcommittees have generally avoided being very directive in report language, for example, specifying or "earmarking" the amount of funding for a particular program or mandating a mechanism, such as centers. The FY2002 report of the House subcommittee, for example, says:

> To enhance NIH's flexibility to allocate funding based on scientific opportunity, the Committee has attempted to minimize the amount of direction provided in the report accompanying the bill. For example, there are

> no directives to fund particular research mechanisms, such as centers or requests for applications, or specific amounts of funding for particular diseases (U.S. Congress, 2001a).

Representative Michael Bilirakis, chairman of the House subcommittee on health, has also expressed reservations about detailed directives to NIH. At a hearing in 2001, he said that the subcommittee had decided not to tell NIH how to spend its appropriation because the members felt that NIH knew where the breakthroughs would occur and would spend the money accordingly (Bilirakis, 2001).

Although the appropriations subcommittees might not mandate centers or their funding, they can communicate preferences in report language. The House and Senate reports for FY2002 appropriations referred to approximately 15 and 25 specific center programs, respectively. The House report generally urged an institute or the NIH director to "enhance" research in an area "through all available mechanisms, as appropriate, including establishing centers of excellence;" "commended" an institute for supporting existing centers; or "encouraged" establishment or expansion of center programs. The Senate report also commended and encouraged use of centers but also used somewhat stronger language ("strongly supports" or "strongly urges" funding of a specific number of new or additional centers). The report strongly urged establishment of at least three centers of excellence for muscular dystrophy research, for example, although a specific number had been dropped from the authorization bill before it became the law.

NIH officials have to decide whether NIH must do something, should do it if possible, or can safely ignore an item in a report, perhaps after contacting the subcommittee to clarify intent. In the case of muscular dystrophy research, NIH decided to set aside funding for two to three centers in the first RFA and announce its intent to issue another RFA to reach a total of at least three centers.

In recent years, the House and Senate authorizing committees have become much more active in passing laws affecting NIH. They have not been able to pass a general reauthorization bill since 1996, because of conflicts over amendments to ban use of fetal tissue and similar issues. Instead, they began to pass narrow bills addressing specific problems. These authorization bills have been the source of recent congressional mandates to create new center programs (e.g., for research on Parkinson's disease, autism, fragile X syndrome, muscular dystrophy, and rare diseases).

The appropriations subcommittees do not have to fund programs created by the authorizing committees, but typically they try to support newly authorized activities. For example, the Senate subcommittee strongly urged NIH to provide "sufficient funds" for "no less than three centers of excellence for basic and applied research in the muscular dystrophies" and for

the three fragile X centers authorized by the Children's Health Act of 2000 and said it wished to see "meaningful implementation of the new Centers of Excellence in Autism Research, mandated in the Children's Health Act of 2000," including the allocation of "sufficient resources" (U.S. Congress, 2001b).[10]

Advisory Group Input

NIH has a standing structure of outside advisory groups and other mechanisms for obtaining outside advice on health needs and scientific opportunities and ideas for new program initiatives. Sometimes, advisory groups recommend establishment of research centers, or they may recommend initiatives the NIH staff decides would best be implemented through centers.

Some advisory groups are standing bodies with rotating memberships from the scientific community and the public, and they play a regular role in the annual program planning and budgeting process and in reviewing programs and new initiatives. These are primarily the national advisory councils, because the substructure of standing program advisory committees has been drastically reduced. Most advisory groups are ad hoc, formed to provide advice on a specific topic, review a particular program, or develop a research agenda for a major area of science.

Each institute and center has a national advisory council or, in the case of NCI, a national advisory board. In most cases, there are 18 members, 12 from the health and scientific disciplines and 6 representatives of the public. The national advisory councils, although advisory, must recommend all research grants awarded by NIH. They are also charged with providing advice on policies and programs, although the arrangements for this are left to the discretion of each institute director (NIH, 1995). Each institute involves its council in the annual program planning and budgeting process and strategic planning exercises in some way. Generally, they participate at several points, providing feedback on priorities and needs early in the process and reviewing and approving concepts for PAs and RFAs to implement new initiatives, including center programs.

NIH leaders also have a number of external advisory committees. The NIH director has the Advisory Committee to the Director (ACD) and the Director's Council of Public Representatives. ACD working groups have reported on gene transfer, clinical research, construction of research facili-

[10]NIH funded three cooperative research centers for the muscular dystrophies in October 2003 and announced plans to establish two more. Two Autism Research Centers of Excellence were funded in May 2002 and seven more in September 2003.

ties, and biomedical computing. The last report resulted in a PAR for planning National Programs of Excellence in Biomedical Computing, supported by 17 institutes, which uses a center mechanism (P20 developmental grants).

Some of the institutes have standing program advisory committees. For example, NCI has an advisory committee to the director, a Board of Scientific Advisers (to oversee extramural programs), and the NCI Director's Consumer Liaison Group. The National Heart, Lung, and Blood Institute (NHLBI) has advisory committees for specific programs (sickle cell disease and sleep disorders). NIAID has similar advisory committees for AIDS research and chronic fatigue syndrome. The institutes used to have more program review committees, but most of these were disbanded in several rounds of advisory committee trimming imposed by several past Administrations.

All the institutes appoint ad hoc bodies (committees, working groups, task forces, or panels) to evaluate programs, assess the state of the science, and develop research agendas. The reports of these groups are another input into the planning process. Sometimes, these groups consider mechanisms and recommend the establishment of centers. For example, an Imaging Sciences Working Group appointed by the NCI director recommended interdisciplinary "imaging centers of excellence,"[11] which resulted in the establishment of In Vivo Cellular and Molecular Imaging Centers.

The institutes convene workshops on a regular basis to help them plan activities in a particular area of science or to address a specific disease or condition. Workshop reports were involved in the genesis of several recent center programs, for example, Centers of Excellence in Chemical and Library Development, Centers for Human Embryonic Stem Cell Research, and Centers of Excellence in Complex Biomedical Systems Research.

Each institute's director and extramural program heads meet regularly with representatives of voluntary health agencies, disease patient advocacy groups, and scientific and medical associations. The NIH director and NCI director meet with their formal consumer advisory groups several times a year. Program staff at all levels participate in annual meetings of scientific and medical associations and some hold focus sessions at these meetings on topics of interest. In addition, some program advisory groups have members representing voluntary health agencies and disease advocacy groups.

In principle, the institutes have extensive ongoing arrangements for obtaining external views and advice from both the research community and the public, and they consult with their national advisory councils on pro-

[11] http://www3.cancer.gov/dip/ISWG3.htm.

gram priorities and balance among mechanisms. In some cases, external committees have created research plans that identify research needs in a particular area and consider the set of mechanisms required to address them, including centers. Increasingly, the strategic plans the institutes develop with external professional and public participation are addressing implementation strategies, including the appropriate mix of mechanisms needed.

Assessment of new program initiatives requires adequate expert advice. The national advisory councils, consisting of scientists, health care providers, and representatives of the public, spend most of their time reviewing applications. They review initiatives and consider the balance among mechanisms, but by the time an initiative reaches the council, it should have been reviewed by expert panels and affected parties consulted. In most cases, the expert review function is carried out by ad hoc advisory groups and either subcommittees of the council or, in several cases (NCI and NHLBI), a board of scientific advisers.

DESIGN AND MANAGEMENT OF CENTER PROGRAMS

During the development of the concept paper and the subsequent PA, RFA, or RFP, NIH staff must make a number of important decisions about the design and management of a center program. These decisions include: how the centers should be organized to achieve the program's goals; how many centers should there be; the maximum award length and size; the mechanism of support to be used; the application review process and criteria; where and by whom will the program be administered within NIH; whether there will be time limits on the program or individual centers; and how the program and individual centers will be evaluated.

Type of Center

NIH supports many types of centers. The center mechanism is very flexible, because the institutes have broad discretion to tailor the goals, requirements, and review criteria in the PA, RFA, or RFP to the specifics of each situation. Broadly speaking, however, NIH offers several major types of center awards, as noted in Chapter 1. One type supports center infrastructure, including the center director and shared services and perhaps other components, such as developmental project funding, leaving it to the center to fund the research by competing for research project funds from NIH and other agencies and organizations. Another type funds research projects as well as shared services and perhaps other programs (e.g., community outreach or professional education). The third type, which is not the focus of this report, supports national or regional centers that provide

research tools (e.g., research resources and materials) to the scientific community in general.

The type of center should, of course, be designed to achieve the program's goals. It should be considered in the process of deciding to establish a center program in the first place.

Number, Size, and Length of Awards

Center grants are, on average, substantially larger than most other awards, and although the award period is usually five years, only a little longer than the award period for RPGs, there are upfront costs of getting a center up and running that make it desirable to maintain it for longer than five years. Centers are intended to provide a stable, long-term focus on an area of research, and they pay for shared facilities and services (cores) if not research projects. The number of centers is sometimes mandated by Congress, but otherwise depends on what the program purpose is, whether related programs exist, and the institute's assessment of the amount of funding needed to assure program effectiveness and whether that level of funding will be available.

Mechanism of Support

NIH has a number of award mechanisms, denoted by activity codes. Some are specifically for centers, such as P30 core grants, P50 and U54 specialized centers, and P60 comprehensive centers. As shown in Chapter 2, however, activity codes are not always used consistently in terms of the types of centers they fund. There appear to be recent trends, however, toward using cooperative agreements (e.g., U54) and toward using noncenter activity codes (e.g., U01 and U19 cooperative agreements, P01 program project grants, and R24 resource-related RPGs).

The trend toward cooperative agreements reflects the desire to facilitate collaborative research among the centers in a program and the desire of NIH to be more involved in programs of great interest to Congress and advocacy groups. Examples among the most recent center programs include the Rare Disease Clinical Research Network (U54), Autism Research Centers of Excellence (U54), and Muscular Dystrophy Cooperative Research Centers (U54). Some are funded by noncenter cooperative agreements, including Breast Cancer and the Environment Research Centers (U01), Centers for Reducing Asthma Disparities (U01), and Cooperative Centers for Translational Research on Human Immunology and Biodefense (U19).

The trend toward awards not classified as center awards stems in part from reviews of center programs that have recommended a shift toward

awards with greater investigator autonomy. Examples include support of population research (from P50 to R24) and research on complementary and alternative medicine (from P50 to P01) (NCCAM, 2002; NICHD, 1999).

In most respects, the activity code does not matter, nor does the presence or absence of the word "center" in the title of the RFA or PA, because the detailed specifications in the PA or RFA determine what the centers will do. There is a significant difference, however, between grants and cooperative agreements. NIH staff are more involved in program planning and decision making in cooperative agreements. But if the center program is expected to include collaborative research, common protocols, and/or development of a national database, the cooperative agreement may be more suitable than grants.

Review Process and Criteria

The review process and criteria for choosing which centers to fund are specified in the PA or RFA or, in the case of some long-standing and well-known programs such as the Cancer Centers, in institute guidelines. In the case of PAs, there are three receipt dates a year for center awards, although the institute may specify a single date. For example, the receipt date for applications for Environmental Health Sciences Core Center Grants is February 1 of each year. RFAs always have a specific one-time receipt date. All applications for center grants and cooperative agreements are reviewed by peer review panels organized by the institute. In some cases, these are standing committees. In most, special emphasis panels are formed on an ad hoc basis to review a particular set of applications.

There may be site visits or "reverse" site visits in which the applicant team travels to NIH to make a presentation. There have been fewer site visits over time, because the funding for administrative overhead has increased less quickly than funding for extramural programs, and the ratio of staff to awards has fallen by nearly half. On the other hand, as mentioned above, there seems to be an increase in the use of cooperative agreements, in which staff participate in project planning and decision making.

The PAs/RFAs differ in how directive they are about research topics to be addressed, how many and what kind of components a center must have, and administrative structure. In the least directive case, they may list potential research areas, but expect each applicant to focus on one, which may be one that was not listed, and then say it is up to the applicant to propose the administrative structure. Or they may be very specific about topics for research projects, the minimum and maximum number of projects, the cores (shared services) that must be provided, and the administrative structure. The RFA for Breast Cancer and the Environment Research Centers,

for example, requires every center to include the same two collaborative research projects, an administrative core, and a community outreach and translation core.

There is also a range of specificity in the review criteria. In a few cases, the only criteria are the basic ones NIH uses for all individual investigator grants, i.e., significance, approach, innovation, investigator, and environment. An example is the RFA for centers of excellence on rare diseases (Rare Diseases Clinical Research Network). In most cases, there are additional criteria. The RFA for the muscular dystrophy centers of excellence has separate criteria for research projects and the shared resource cores, as well as another dozen criteria specific to the Muscular Dystrophy Cooperative Research Centers program. The RFA for Cooperative Research Centers for Translational Research on Human Immunology and Biodefense has separate criteria for (1) organization and scientific potential of the center, (2) research resource technical development component, (3) research project component, (4) core facilities component, (5) pilot project component; and (6) education component.

Program Administration

There are several models of extramural center program administration. In some cases, there is a central office responsible for administering the center program. This is generally the case in which the institute has a single center program that is meant to be a platform for all the institute's extramural programs. Examples include NCI's Cancer Centers and NEI's Vision Centers. The Alcohol Research Centers were recently moved to the National Institute on Alcohol Abuse and Alcoholism's (NIAAA's) Office of Collaborative Research Activities.

In other cases, institutes have several center programs, each administered in the relevant extramural program division. The advantage of the latter arrangement is that all the mechanisms the institute uses in a specific area—e.g., individual investigator grants, program projects, centers, small business grants, career development grants, and research and development contracts—are planned and administered together, which should increase program coherency and help assure appropriate use of centers. NIGMS, for example, established a Structural Genomics and Proteomics Technology Branch in the Division of Cell Biology and Biophysics to administer the research centers and research grants constituting the Protein Structure Initiative.

The disadvantage of putting centers with other programs in separate divisions and branches may be the limited time and resources the program staff has to oversee the centers along with other types of grants and contracts. In centralized center programs, full-time staff may manage the pro-

gram more effectively, but the coordination of centers with related activities is more difficult.

Sometimes, there is an external advisory body to the center program. There is a Cancer Centers subcommittee of the National Cancer Advisory Board. For NIAAA's alcoholism centers, a separate advisory committee was set up under the National Advisory Council on Alcohol Abuse and Alcoholism.

Time Limits or Sunset Provisions

Some institutes (e.g., NIMH) have adopted a general policy of allowing one five-year renewal after the first five-year award to an individual center. For example, in the case of Centers of Excellence in Chemical Methodologies and Library Development, the RFA says no center will receive more than 10 years of funding, "either because the project goals will have been accomplished or the Center will have developed to the point that support from other sources will be more appropriate."[12] In another case—Centers of Excellence in Genomic Science—the PA says the institute will conduct an administrative site visit in the third year of a center grant to determine if there will be a fifth year of funding and to advise the Principal Investigator about the "interest" of the National Human Genome Research Institute "in accepting a competing renewal application to extend the initial award."[13]

No institutes have sunset provisions for center (or other) programs, except NHLBI, which in 1993 adopted a policy of limiting each Specialized Center of Research (SCOR) program to 10 years of funding "unless a thorough evaluation of research needs and opportunities uncovered extraordinarily compelling reasons to continue a specific SCOR program" (Lenfant, 2002).

Funding Limits

Institutes usually impose a limit on the amount of first-year funding for direct costs or total costs for new centers and the percentage increases they may request in subsequent years of the award period. Competing renewal centers are usually limited in the percentage increase they may ask for.

Evaluation Requirements

Evaluation of center programs as programs is addressed in Chapter 5. Concerning evaluation of individual centers, the main tool is prospective

[12]RFA-GM-03-004.
[13]PAR-02-021.

evaluation, that is, review of the application for competitive renewal at the end of each award period, which is usually five years. The focus of the evaluation is on the merit of the proposed activities to be supported by the renewal grant, although past productivity, especially publications in peer-reviewed journals, is also considered. There may be a site visit or, because of budget constraints on NIH administration, a reverse site visit. There is an annual noncompetitive renewal decision, but it is based on a written annual report and perhaps a site visit by the NIH program officer. Some RFAs require the application to include an evaluation plan and require formation of an external advisory committee, one of whose duties is to oversee the evaluation plan process.

FINDINGS AND RECOMMENDATIONS

NIH has long supported research centers to achieve a number and variety of defined scientific and programmatic objectives that cannot be achieved, or achieved as well or as quickly, by individual laboratories or informal collaboration. These objectives include encouraging interdisciplinary research and research training, fostering translational research, providing research resources and facilities cost-effectively to individual investigators, developing research infrastructure in fields or institutions that have not been research intensive, providing a regional resource for health care providers or first responders, and supporting a network of centers able to recruit adequate numbers of patients for clinical research and clinical trials.

Finding. Proposals to establish center programs originate from many sources within and outside NIH, including scientific workshops, internal program reviews, national advisory councils and other advisory bodies, NIH professional staff, professional scientific societies, citizen groups, the executive branch, and Congress. Although each of the institutes has a planning process for setting priorities and developing programs, the procedures and criteria for assessing the appropriateness of centers in an area of research are not explicit or uniform. The national advisory councils are currently required to review all initiatives, but given the small amount of time they can devote to the task, effective arrangements for soliciting external advice in the approval process and clear and consistent criteria for program approval (see next recommendation) are critical elements of center program initiation.

Recommendation 2. NIH should make explicit its process for deciding whether establishment of a new center program is appropriate to meet a specified goal. The key elements of the process, which should be

consistent across institutes, necessarily involve broad input from the extramural scientific community and incorporation of the views of the public. NIH needs to inform Congress and advocacy groups of the process and of the opportunities they will have to provide input.

Implementation of the new process should be overseen by the NIH director or someone he or she designates. The process (and criteria) for establishing center programs would, however, continue to be applied at the institute level.

Currently the program planning process is driven by the annual federal budget process, which fosters incrementalism rather than broad, long-term planning. The virtue of a long-range strategic planning process is the broad context it provides in which to consider the balance among mechanisms (e.g., research program grants, centers, training, contracts, etc.). The question becomes one of the best mix of approaches to take to major problems rather than whether one mechanism is "better" than another. The institutes should consider making it standard practice in their strategic plans to include an assessment of the mechanisms needed to achieve the strategic goals identified in the plans. This is similar to but not the same as portfolio analysis, which is an approach to priority setting and program balancing that should focus on the content of the scientific program, not the mechanisms which implement them.

Given the decentralized process for program planning at NIH, the new process should lead to more consistency in justifications of new center program initiatives, clearer identification of the number and funding of center program awards, and better evaluations of the effectiveness of center programs. The process will benefit NIH by being more open and understandable to the public. At the same time, the specifics of the PA or RFA will leave adequate flexibility to tailor requirements to the particular needs in each case.

REFERENCES

Bilirakis M. 2001. Remarks at "Advancing the Health of the American People: Addressing Various Public Health Needs." Hearing before Subcommittee on Health of the House Committee on Energy and Commerce, June 27, 2001, as reported by the NIH Office of Legislative Policy and Analysis. [Online]. Available: http://olpa.od.nih.gov/OLPAReports/062701PubHlth.htm [accessed October 30, 2001].

Dorman D. 2001. Statement of the Senior Director for Public Policy of the National Organization for Rare Disorders at the March 14, 2001, hearing of the Subcommittee on Labor, Health and Human Services, Education and Related Agencies of the U.S. House Committee on Appropriations, U.S. House of Representatives. [Online]. Available: http://www.rarediseases.org/news/speeches/house [accessed December 15, 2003].

Hagerman RJ. 1999. *On behalf of H.R. 1445, Fragile X Research Breakthrough Act of 1999*. Statement before a 1999 hearing of the House Subcommittee on Health and Environment. Reprinted in: *National Fragile X Foundation Quarterly*, Fall 1999. Pp. 9-10. [Online.] Available: http://www.nfxf.org/html/news1999.htm# [accessed December 15, 2003].

IOM (Institute of Medicine). 1991. *Mapping the Brain and Its Functions: Integrating Enabling Technologies into Neuroscience Research*. Washington, DC: National Academy Press.

Kennedy EM. 2001. Statement on the Senate floor when introducing the Rare Diseases Act of 2001. *Congressional Record*, 107th Congress, 1st Session, August 3, 2001. Pp. S8952-S8953.

Lenfant C. 2002. Strengthening commitment to clinical research: The National Heart, Lung, and Blood Institute's Specialized Centers of Research program. *Circulation* 105(4):400-401. [Online]. Available: http://www.nhlbi..nih.gov/funding/fromdir/circ-1-02.htm [accessed December 15, 2003].

National Commission on Orphan Diseases. 1989. *Report of the National Commission on Orphan Diseases*. Publication Number HRP-090-7248. Washington, DC: U.S. Government Printing Office.

NCCAM (National Center for Complementary and Alternative Medicine). 2002. *Research Centers Program Expert Panel Review*. [Online]. Available: http://nccam.nih.gov/about/plans/centers/report.pdfx [accessed January 8, 2003].

NIAID (National Institute of Allergy and Infectious Diseases). 2002. *NIAID Strategic Plan for Biodefense Research*. [Online]. Available: http://www.niaid.nih.gov/biodefense/research/strategic.pdf [accessed December 15, 2003].

NIAMS (National Institute of Arthritis and Musculoskeletal and Skin Diseases). 2002. "Summary of the First Meeting of the NIH Muscular Dystrophy Research Task Force, held May 15-16, 2002," Bethesda, MD. [Online]. Available: http://www.niams.nih.gov/ne/reports/sci_wrk/2002/mdmeet.htm#agenda [accessed December 15, 2003].

NICHD (National Institute of Child Health and Human Development). 1995. "Recommendations of the Working Group on Medical Intervention," in *State of the Science in Autism: Report to the National Institutes of Health*. [Online]. Available: http://www.nichd.nih.gov/publications/pubs/autism/sub8.htm [accessed December 15, 2003].

NICHD. 1999. "Report of the Demographic and Behavioral Sciences Branch Population Centers Review." [Online.] Available: http://www.nichd.nih.gov/about/cpr/dbs/pubs/report.pdf [accessed December 15, 2003].

NIGMS (National Institute of General Medical Sciences). 1998. *New Approaches to the Study of Complex Biological Processes*. Report of a workshop held by NIGMS in November 1997. [Online]. Available: http://www.nigms.nih.gov/news/reports/complexbio.html [accessed December 15, 2003].

NIGMS. 2000. *Diversity-Oriented Synthesis Meeting*. Report of a workshop held by NIGMS in August 2000. [Online]. Available: http://www.nigms.nih.gov/news/reports/chemical_diversity.html [accessed December 15, 2003].

NIGMS. 2002. *Workshop on the Basic Biology of Mammalian Stem Cells*. Report of a workshop held by NIGMS in June 2002. [Online]. Available: http://www.nigms.nih.gov/news/reports/stemcellworkshop.html [accessed December 15, 2003].

NIH (National Institutes of Health). 1995. Management and procedures of national advisory councils and boards in their review of extramural activities. In: *NIH Policy Manual,* Chapter 4513. Bethesda, MD: NIH (Available from the Office of Extramural Programs, Office of the Director, NIH).

NIH. 1999. *Report on Steps to Coordinate Rare Diseases Research Programs: Analysis by and Recommendations of the Special Emphasis Panel of the National Institutes of Health on the Coordination of Rare Diseases Research*. [Online]. Available: http://rarediseases.info.nih.gov/html/reports/fy1999/SEP.html [accessed December 15, 2003].

NIH. 2001a. *Congressional Justification for FY2002*. Bethesda, MD: NIH. Office of Financial Management: Vol. 1, Overview.

NIH. 2001b. *Setting Research Priorities at the National Institutes of Health*. Revised edition. [Online]. Available: http://www.nih.gov/about/researchpriorities.htm [accessed December 15, 2003].

U.S. Congress. 2001a. H.R. 3061, Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriation Bill, 2002. House Report 107-229. Washington, DC.

U.S. Congress. 2001b. S. 1536, Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriation Bill, 2002. Senate Report 107-84. Washington, DC.

U.S. Congress. 2001c. "Muscular Dystrophy," Hearing before the Senate Appropriations Subcommittee on Labor, Health and Human Services, and Education, February 27, 2001.

4

Criteria for Establishing Center Programs

It is evident from the description of the National Institutes of Health (NIH) planning and budgeting process in Chapter 3 that proposals to establish new initiatives such as a center program are vetted extensively by external advisors as well as professional staff and weighed against other priorities and mechanisms of research support. Clearly there are criteria for adopting center programs—new center programs are not established without considerable effort and on occasion they are revised and even terminated in response to changing circumstances—but the decision criteria are implicit and somewhat variable from institute to institute. There are no official NIH-wide criteria for establishing center programs. The institutes also do not have published criteria for center programs.

The major reason that the definitions of research centers and the criteria for establishing a center program at NIH are not very specific or standardized stems in part from their varied nature. Centers are a means to an end—advancing research in a particular area of science—and the need for a center depends in part on the opportunities and needs in that area. The absence of explicit criteria for establishing a center program is reinforced by the format in which the choice is presented—i.e., as a concept paper for a particular type, number, and size of center. The paper is often written as a draft of the substantive sections of the Program Announcement (PA) or Request for Applications (RFA) that will be issued if the program is approved and funded, rather than as a response to criteria for creating a program.

The benefit of implicit criteria is flexibility. An institute or group of

institutes can establish a new initiative to support projects that function like a center, but call them something else, such as programs, collaborative projects, networks, partnerships, initiatives, teams, or consortia.[1] There is also flexibility in the mechanism of support. Most center programs use center grants or cooperative agreements to support centers, but some use research project grants (RPGs) or research and development contracts.[2] Whatever the mechanism of support the program uses, the requirements in the solicitation can be tailored to each situation, depending on the desired role of centers in a specific area of research.

The lack of explicit and consistent criteria, however, can be a source of frustration for those on the outside—citizen and professional groups and congressional overseers—who may not be sure why NIH establishes, or opposes establishment of, centers as an appropriate mechanism for productive research. This chapter analyzes the criteria implied in the justifications for center programs published in the invitations for applications (PAs and RFAs). The committee believes that developing and adopting explicit criteria would improve decision making and make it more understandable and acceptable to interested parties outside NIH.

IMPLIED CRITERIA FOR CENTER PROGRAM ESTABLISHMENT

Review criteria for evaluating applications for center awards are published in the PAs and RFAs, but they address the specific purpose of each particular set of centers and, in any case, the criteria for selecting award winners are not the same as those for deciding whether the program of awards is appropriate in the first place. For example, a common criterion for establishing a center program at NIH has been the need for multidisciplinary research on a problem by scientists in different fields who

[1]See, for example, Specialized Programs of Research Excellence (P50). NCI; Biodefense Proteomics Research Programs (N01), NIAID; Large-Scale Collaborative Projects (U54), NIGMS; Biomedical Research Infrastructure Network (P20), NCRR; Rare Disease Clinical Research Network (U01), NCRR-ORD-NINDS-NICHD-NIAMS-NIDDK; Network for Translational Research: Optical Imaging (U54), NCI; Excellence in Partnerships for Community Outreach, Research on Disparities in Health and Training (Project EXPORT), (P60), NCMHD; Protein Structure Initiative (P50), NIGMS; National Heart, Lung, and Blood Institute Proteomics Initiative (N01), NHLBI; Interdisciplinary Research Teams for Molecular Target Assessment (U54), NCI.

[2]See, for example, Centers for Children's Environmental Health and Disease Prevention Research (P01), NIEHS; Cooperative Centers for Translational Research on Human Immunology and Biodefense (U19), NIAID; Breast Cancer and the Environment Research Centers (U01), NIEHS-NCI; Autoimmunity Centers of Excellence (U19), NIAID-NIDDK-ORWH; Asthma and Allergic Diseases Research Centers (P01), NIAID; Centers for Reducing Asthma Disparities (U01), NHLBI.

do not usually collaborate. A criterion, therefore, for selecting an application for a center grant from this program would be whether the applicant shows convincingly that he or she would in fact be able to create the multidisciplinary collaboration the program was established to achieve. The criterion for establishing the center program in the first place would have been that a high-priority research question could only be addressed by multidisciplinary research on a scale that individual laboratories could not achieve working separately.

The only NIH-wide application of criteria for a new center program is the procedure used in reviewing and approving concepts for PAs and RFAs for any new program initiatives. The NIH *Manual* says that concepts must be reviewed for "relevance, priority, and need" by the institute's national advisory council or other advisory body (NIH, 1994). If the awards are going to be cooperative agreements, the institute must also justify the rationale and need for substantial scientific and programmatic involvement by NIH staff in the program (NIH, 1993). These criteria apply to new centers because they are always launched, at least initially, by an NIH initiative.

There are also several definitions of centers. According to a glossary of NIH grant terms, "Research Centers" are "Grants that support multidisciplinary, long-term research and development programs at research centers. Research centers usually have a clinical orientation and include all P activities … that are not included in research projects (R); M01 activities; selected U activities (U41, U42, U54); R07; and G12."[3] The reference to letters and numbers refers to activity codes in the codebook for Information for Management, Planning, Analysis, and Coordination (IMPAC), NIH's management information system (NIH, 2002), which the Office of Extramural Programs uses to track the number and funding of awards. Each code has a short definition, but these were not intended to form the basis for criteria for deciding whether centers are needed. Also, although some institutes post the IMPAC definitions on their website, others have their own definitions. The National Institute of Child Health and Human Development (NICHD), for example, has its own definition of the P50 grant.[4] The National Cancer Institute (NCI) adopted the IMPAC definition for the P50 specialized center in the list of extramural mechanisms on its website, but in practice it uses the grant selectively to support centers focusing on translational research. NCI uses the P50 code for its Specialized Programs of Research Excellence (SPORE) and has modeled its newer center programs on what it calls the SPORE "blueprint," such as Transdisciplinary

[3]grants.nih.gov/grants/glossary.htm.
[4]www.nichd.nih.gov/funding/mech_research.htm#p30.

Tobacco Use Research Centers and Centers of Excellence in Cancer Communications Research (NCI, 2001, 2002).

RFAs and PAs often state the rationale for a center program, usually in a few sentences in the opening paragraph, which states the purpose of the RFA or PA, although the focus is on the criteria for funding centers rather than the criteria for establishing the center program. Sometimes they refer to institute or trans-NIH priorities or strategic goals or to recommendations of an expert group or workshop. They may say that centers are better suited to accomplish program goals than other types of research support, such as traditional individual investigator-initiated grants or program project grants. Some discuss how centers combine with or complement other mechanisms to advance research in a field or on a problem.

The justifications for center programs used in RFAs and PAs can be grouped into the following categories, which are in effect the implied criteria in common use.

1. The scientific opportunities and/or public health needs that the program would address have high priority.

A center program is more expensive, represents a long-term commitment, is more complex to administer and evaluate, and leaves the institute with less budget flexibility than the traditional research grant. The problem or opportunity it would address, therefore, should be especially important, in principle identified or reviewed by outside advisors and made a high program priority by the institute's leaders and national advisory council or meet a trans-NIH priority. RFAs and PAs for centers typically devote a paragraph or two to the importance of the research the center program is expected to facilitate, usually referring to a priority-setting exercise, such as a strategic plan, institute or NIH initiatives, or advisory group report on research priorities. A program of centers is often intended to be part of a set of activities that complement if not reinforce each other, including individual and program project grants, clinical trial networks, career development and training grants, and access to research resources supported by NIH.

According to the RFA for Centers of Excellence in Complex Biomedical Systems Research, for example, "This program is responsive to the Biomedical Information Science and Technology Initiative and its call for National Programs of Excellence in Biomedical Computing…The NIGMS [National Institute of General Medical Sciences] intends to support Centers of Excellence in Complex Biomedical Systems for research areas that 1) are central to its mission, and 2) focus on developing new computational approaches to biomedical complexity…An example of particular interest to NIGMS has been articulated in the planning document, 'A Vision for the

Future: A Complete Picture of the Healthy Cell.'"[5] Additional examples of justifications of center programs based on the importance of the scientific opportunities or public health needs, or both, that they would address, are in Appendix E.

2. The center would provide an organizational environment that would facilitate activities that are most effectively undertaken by teams of investigators working in close proximity.

These activities include:

- *multidisciplinary collaborations for problems that require diverse scientific backgrounds*

Every PA and RFA examined by the committee states that multidisciplinary or interdisciplinary research was a major reason for creating centers. Some noted that centers provide an environment more conducive to multidisciplinary research on complex problems than individual investigator grants. Some PAs and RFAs stated that centers would make faster progress in multidisciplinary research than individual investigators working separately would.

The RFA for Muscular Dystrophy Cooperative Research Centers, for example, states that "Muscular dystrophy research requires multidisciplinary approaches, based on expertise in muscle biology, genetics, imaging, muscle plasticity, exercise science and physical therapy, nutrition, molecular biology, neuroscience, rehabilitation medicine, epidemiology, clinical trials, bioengineering, electrophysiology, psychology, and behavioral sciences."[6] Similar statements in other RFAs are quoted in Appendix E.

- *multi-investigator teams capable of a scope of activities not possible with other funding mechanisms*

Many centers consist of basic, clinical, and population-based research projects that are supposed to focus on a common theme and interact to promote translation of basic research findings into clinical applications. In some cases, centers are meant to enable assembly of research teams that can tackle research questions too large for other types of research support to handle easily.

[5]RFA-GM-01-001.
[6]RFA-AR-03-001.

The PA for Cooperative Centers for Translational Research on Human Immunology and Biodefense put it this way: "The Cooperative Agreement mechanism (U19)…will be used to support the development of multi-investigator teams with a scope of activities not possible with other funding mechanisms."[7] Similar statements from other PAs and RFAs are in Appendix E.

- *translating the results of basic research into clinical practice*

Many recent centers are expected to engage in translational research, which is the bridge between basic science and better treatments, diagnoses, and prevention efforts. Translational research moves basic research advances into technology development and initial clinical trials while basic researchers benefit from proximity to patients and clinical research. For example, "The major goal of this program [Autoimmunity Centers of Excellence] is to support an integrated basic and clinical research program focused on tolerance induction and immune modulation to prevent or treat autoimmune disease. The close interaction between basic researchers and clinicians will accelerate the translation of basic advances to the clinic and the utilization of patient materials for basic research."[8]

- *complementing existing and stimulating new investigator-initiated applications for research project grants*

Core grants, which fund research resources and services, called "cores," and center administration, but do not fund investigators or research projects, are meant to support researchers funded by other means. Even when the center grant funds research projects, such as a P50 award, the RFA often indicates that the centers are supposed to complement and interact with RPGs and other mechanisms of support. Some larger established center programs, for example, Cancer Centers, are designed to serve as a nationally distributed platform for an institute's broader portfolio of programs (e.g., individual investigator and other types of grants; training programs; clinical trials; screening and prevention programs; and community education, outreach, and intervention programs). A recent external review of the Cancer Centers program urged NCI to increase its reliance on centers for program implementation and coordination (NCAB, 2003).

[7]RFA-AI-02-042.
[8]RFA-AI-02-006.

Centers for AIDS Research and Alzheimer's Centers, among others, also carry out this function. The new Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research of NIAID will be regional resources, providing biosafety level 3 and 4 containment facilities and backing up first responders in an emergency.

The RFA for Autism Research Centers of Excellence stresses the complementarity of center grants and other forms of research support. "STAART [Studies to Advance Autism Research and Treatment] support is not intended to be a substitute for individual grant support. It is, therefore, expected that project and core leaders will have independent, peer-reviewed research support. Neither should the STAART Center be the primary source of research funding for the investigators associated with the Center. It is desirable for STAART-supported research to complement other funded research related to autism taking place at the applicant institution, including activities supported by R01, P01, P30, P50, and other mechanisms."[9] For other RFAs that indicate the center program is supposed to complement the institute's other mechanisms of research support, see Appendix E.

- *training of graduate students, postdoctoral fellows, physician-scientists, nurses, and other health professionals in cross-disciplinary or translational research*

In some cases, a center is expected to promote training in the area of research the center addresses, although few center awards fund training activities or support trainees. For example, Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research "must include a consistent and significant commitment to career development with the goal of increasing the availability of researchers for biodefense. This may focus on advanced postdoctoral candidates, junior faculty, or established investigators who wish to develop or refocus their careers on biodefense research."[10]

- *attracting experienced researchers into a new area of research*

The existence of a center is also expected to attract established researchers into the field that is the center's focus. The purpose of Exploratory Center Grants for Human Embryonic Stem Cell Research, for example, is to "encourage and enable basic biologists with little or no prior

[9]RFA-MH-02-001.
[10]RFA-AI-02-031.

HESC [Human Embryonic Stem Cells] experience to work with HESC and establish the utility of HESC as a model system."[11]

- *networking with other centers in the program to conduct coordinated research beyond the capacity of any single center, for example, by recruiting larger numbers of patients into common research protocols; pooling patient data and biological specimens on the scale necessary to identify biomarkers for disease risk, disease activity and severity, and clinical outcome; and improving methods and technologies*

There is a trend in recent center programs toward considering the set of centers not just on their own, but as a network or consortium of centers with the capacity to collaborate on activities that cannot be accomplished by individual centers. In some cases, the program sets aside funding for collaborative research projects and establishes a steering committee of representatives from the centers and NIH to identify opportunities and set priorities for the funding of collaborative projects. This probably reflects the increasing scale of research in many areas of health research. It also reflects the establishment of center programs addressing relatively rare diseases, where multiple sites are needed to recruit enough patients for translational and clinical research.

In the case of Breast Cancer and the Environment Research Centers, for example, "All study sites will use similar methods to collect data on markers of physiologic changes during the pubertal process, and assessment of environmental stressors of importance to future breast cancer risk, including lifestyle behaviors, nutrition and anthropometric markers, and chemical, physical, and social exposures at home and school. In addition, pooled analysis of genetic polymorphisms of interest will be included to fully explore relevant gene–environment interactions."[12]

3. The centers would provide critical research resources needed for productive research that are difficult or too expensive to develop in most individual laboratories.

In the case of core grants, usually the majority of funding supports research resources and services that can be provided to investigators on a more cost-effective basis than alternative mechanisms can. Such resources are not unique to core grants. For example, program project (P01) grants

[11]RFA-GM-03-003.
[12]RFA-ES-03-001.

also support cores, but in most institutes they are smaller in budget and number of projects allowed than center awards.

Institutional Center Core Grants to Support Neuroscience Research are an example of a center program established to provide critical research resources. "The purpose of this program is to advance the NINDS [National Institute of Neurological Disorders and Stroke] mission to promote understanding and treatment of neurological disorders by providing core research facilities that are not otherwise available. Each Center Core Grant will support shared resources and facilities used by investigators with research projects funded by NINDS. This support, by providing more accessible resources, is expected to assure a greater productivity than would be possible from the separate projects."[13]

4. The centers would build the infrastructure to promote the institutional development of a field of research (e.g., nursing, population research) at minority-serving institutions or institutions in regions with little NIH research funding and community education and outreach programs.

Sometimes, a center program is a deliberate strategy to build up a field or area of research. The National Institute of Nursing Research, for example, "has historically supported the development of research infrastructure in schools of nursing by funding Centers," according to its RFA for nursing research developmental center grants.[14] NICHD started the population research centers program 30 years ago to support researchers when population research was a developing field. Now that the centers are well established, NICHD has changed the program to develop population research infrastructure in new places.

Center programs have been established recently to build research capacity in minority institutions as part of a strategy to address health disparities. These include the National Center for Minority Health and Health Disparities' Project EXPORT centers; Comprehensive Centers on Health Disparities funded by the National Center for Research Resources (NCRR) and National Institute of Mental Health; NCRR's Centers of Biomedical Research Excellence; Centers for Population Health and Health Disparities funded by the National Institute of Environmental Health Sciences, NCI, National Institute on Aging, and Office of Behavioral and Social Science Research; and Native American Research Centers for Health co-funded by NIGMS and the Indian Health Service. The RFA for Excellence in Partner-

[13]PAR-02-059.
[14]RFA-NR-04-001.

ships for Community Outreach, Research on Disparities in Health and Training (Project EXPORT) put it this way: "These center grants will provide a mechanism to strengthen the infrastructure for minority health and other health disparities research and training as well as provide resources for the development of innovative partnership models."[15]

FINDINGS AND RECOMMENDATIONS

NIH has supported research centers to achieve a number of scientific and programmatic objectives. These include encouraging interdisciplinary research and research training, fostering translational research, providing research resources cost-effectively to individual investigators, developing research infrastructure in fields or institutions that have not been research intensive, providing a regional resource for health care providers or first responders, and supporting a network of centers able to recruit adequate numbers of patients for clinical trials or other research protocols.

Finding. The rationale for initiating a center program stated in concept papers or in the PAs and RFAs does not always indicate why a program of centers is a better means for achieving program goals than other mechanisms of research support. The scientific rationale for adding centers to the mix of funding mechanisms in a specific area is not usually made explicit, and the comparative advantage of using centers to accelerate progress is not always shown.

Recommendation 3. A uniform set of key questions to ask in establishing each program of centers, such as those listed in Box 4-1 below, should be developed and adopted by NIH. The recommendation to establish any program of centers should be supported by positive responses to the relevant questions on the list that NIH adopts.

Acceptance and use of explicit and consistent criteria such as these by all interested parties, including Congress, patient advocacy groups, and the scientific community as well as NIH, would contribute to a more informed discussion and improved decision making concerning the appropriate use of centers or other mechanisms of research support in carrying out the NIH mission. At the same time, we believe that the criteria, such as those suggested above, should not be so narrow and detailed that they inhibit creativity and needed flexibility in addressing the wide range of research questions that NIH faces. As with Recommendation 2, the goal is to provide

[15]RFA-MD-02-003.

BOX 4-1
Suggested Criteria for Initiation of Center Programs

	Center program may be the right mechanism if…	Another mechanism is more appropriate if…
Both Center Infrastructure (Core-Type) and Research Center Programs Should Meet the Following Criteria.		
Importance of the problem: Is the area of research important enough to warrant a concentration of resources?	The area of research has been declared a high priority by the institute in its planning process.	The area of research is a lower priority for the institute.
Need for core resources: Do shared resources in this area provide economies of scale?	The area of research relies heavily on specialized resources not provided in normal university services but difficult to include in research project or program project (i.e., R01 or P01) budgets.	The area of research can proceed with standard university services, or individual investigators can access the services cost-effectively.
Center Infrastructure (Core-Type) Programs Should Meet the Following Additional Criteria.		
Concentrations of projects: Do enough investigators at one university or in close proximity already have funded projects in this area?	The proposed program or award can justify in detail that there are enough users for the shared services.	The number of documented potential users is well below the capacity of the proposed shared resources.
Research Center Programs Should Meet the Following Additional Criteria.		
Sufficient number of investigators: Are there enough people working in the field to support the level of effort proposed?	There are, or potentially are, plenty of strong investigators in the area, so that there will be real competition for the center awards.	There are few investigators, or little potential for more investigators working in development with noncenter grants.

Need for strategic focus: Does this research area need some coordination among projects to build toward or accelerate important findings?	Scattered findings from a number of research groups are leaving critical gaps in the knowledge base. These groups need to articulate a larger-scale, more coordinated research program to make or accelerate progress.	Individual grants or P01s are already moving the field forward rapidly based on shared understanding of the critical methods and problems.
Need for interdisciplinary interaction: Would the research problem benefit from an interdisciplinary approach that is not happening now?	Current grant-supported research is largely single-discipline, and credible, independent advisors recommend an interdisciplinary approach.	Current R01 and P01 research is already interdisciplinary.
Need to identify research problems with translational potential: Does the clinical community perceive that their problems are not being addressed?	The clinical or other practice community can provide a significant body of questions that research could address to help them solve problems but is not currently producing. The list of questions should be articulated, and the match against existing knowledge should be documented with a literature search.	The clinical or other practice community is already absorbing a high level of research knowledge and has significant influence on the research agenda of basic research related to the problem.
Need to stimulate translational activities: Does the basic science community perceive that their findings are not being taken up?	There is a large body of knowledge that is not being translated into clinical or public health practice. The program should be able to quantify the size of that body of knowledge with publications.	Basic research related to the problem is already being fully utilized in clinical research, drug development, clinical practice, or public health.
Need to provide distinctive training environments	Researchers trained in existing modes in the field are being prepared too narrowly to meet the challenges of problem solving in this area, or are missing critical skills.	Existing training is giving Ph.D.s and physicians the key skills and knowledge they need for their career paths.

enough structure to produce transparency, but not so much as to inhibit creativity.

Finding. NIH is occasionally urged to establish centers by Congress or by groups advocating greater federal action on a specific disease or other health issue about which NIH scientists believe the knowledge base or the number of active researchers, or both, are too small to support an effective center program. Even if the process and criteria for reaching this conclusion are made more open and explicit, and involve broad input from the scientific and advocacy communities (see Recommendation 2), differences among stakeholders and scientific experts may still exist. Congressional hearings may not provide the optimal forum for resolving these differences. A need exists for an advisory mechanism to assist Congress and NIH when there is continuing disagreement about the need for centers for a specific disease or other health problem.

Recommendation 4. In those occasional instances in which disagreement continues over the need to establish a new center program, the NIH director or congressional committee chairman could request that an advisory committee be appointed by the Secretary of Health and Human Services to review the evidence in support of a developing initiative for a centers program and assess whether the proposed program meets the prestated criteria for the establishment of centers.

The committee does not believe that the ad hoc review process will be used often. Historically, appropriate responses to public health needs have been worked out, sometimes including establishment of a center program. Relatively few center programs have been mandated by Congress. Congress should be the court of last, not first, resort. Congress should first consider whether the process, like the one recommended in the last chapter (Recommendation 2), which would ensure broad input and consideration of the need for centers, has been followed by NIH, and whether criteria like the ones recommended above (Recommendation 3) have been applied, which would ensure that the costs and benefits of the center model have been weighed against other ways of supporting research. If the open process and appropriate criteria have been followed, that is, if all arguments for establishing centers have been heard and the criteria for centers have been applied as part of the NIH program planning and budgeting process, but the responsible officials at NIH—ultimately the NIH and institute director or directors—decide that a center initiative is not an appropriate response to the biomedical problem in question, Congress may be assured that a decision that new centers are not needed is well justified.

REFERENCES

NCAB (National Cancer Advisory Board). 2003. *Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future*. Report of the National Cancer Advisory Board Ad Hoc P30/P50 Working Group. [Online]. Available: http://deainfo.nci.nih.gov/ADVISORY/ncab/p30-p50/P30-P50final12feb03.pdf [accessed December 15, 2003].

NCI (National Cancer Institute). 2001. *Guidelines for Specialized Programs of Research Excellence (SPOREs)*. [Online]. Available: http://deainfo.nci.nih.gov/awards/spore.htm [accessed December 15, 2003].

NCI. 2002. *Plans & Priorities for Cancer Research: The Nation's Investment in Cancer Research for Fiscal Year 2004*. [Online]. Available: http://plan.cancer.gov/ [accessed December 15, 2003].

NIH (National Institutes of Health). 1993. Implementation of Cooperative Agreements. In: *NIH Policy Manual,* Chapter 4815. Bethesda, MD: NIH (Available from the Office of Extramural Programs, Office of the Director, NIH).

NIH. 1994. Program announcements and requests for applications. In: *NIH Policy Manual,* Chapter 4110. Bethesda, MD: NIH (Available from the Office of Extramural Programs, Office of the Director, NIH).

NIH. 2002. *Activity Codes, Organization Codes, and Definitions Used in Extramural Programs*. [Online]. Available: http://grants.nih.gov/grants/funding/ac.pdf [accessed December 15, 2003].

5

Evaluation of Center Programs

The National Institutes of Health (NIH), like other federal research agencies, takes several approaches to evaluating the performance of its programs. One is technical review by a panel of external experts knowledgeable in the area of research involved and perhaps users of the research results. Another approach is formal evaluation based on data collected by external contractors.

As described in Chapter 3, a proposal to establish a program of research centers in the first place undergoes a prospective review process, which varies from institute to institute but generally involves an external committee or workshop to obtain input on the goals and design of the proposed centers as well as the required review and approval by a chartered external advisory body (usually the institute's national advisory council) and clearance of the Request for Application (RFA) or Program Announcement (PA) through the Office of Extramural Programs in the Office of the Director of NIH.

Research programs may also undergo retrospective evaluation. Each ongoing as well as proposed center program must justify itself in the annual planning and budgeting process. In addition, some of the institutes engage in a formal "visiting committee" process, that is, an external panel of experts, usually a subcommittee of the institute's national advisory committee for a major program division that reviews the division's programs on a regular schedule. The National Institute on Aging's national advisory council, for example, reviews three of the institute's six major program units each year, one at each of its first three meetings of the year. This process can

lead to changes in center programs or proposals to initiate new center programs.

In one case, the institute has a time limit, or "sunset" provision, when a major external review must be conducted to determine if the center program should be continued. As noted in Chapter 3, the National Heart, Lung, and Blood Institute (NHLBI) has a 10-year limit on each of its Specialized Centers of Research/Specialized Centers of Clinically Oriented Research programs (each of which supports several centers for research on a specific disease), at which time they are replaced by a new program on another disease, unless a committee of outside experts determines that there are "extraordinarily compelling reasons" to continue the program (Lenfant, 2002). Some other institutes have 10-year limits (e.g., two 5-year awards) on individual centers, but not on the overall program.

From time to time, institute staff members, the institute director, or the national advisory council decides that a center program should be reviewed by staff, an external committee of experts, or a combination of staff and outside experts for its continuing effectiveness and/or relevance. Examples of reports from such ad hoc exercises are summarized in Appendix E. Generally the reports are based on the experience and expert judgment of committee members, because for reasons discussed below, objective measurement and analysis of a program's performance, especially in terms of outcomes and impact, are difficult to perform and frequently require resources and technical skills beyond that provided to the committees. More sophisticated evaluation designs, such as those involving comparison groups, are generally viewed as even more difficult to perform and, therefore, are seldom employed in practice.

These exercises are also basically what are called formative or process evaluations (which assess the ongoing program process to identify modifications and improvements) rather than summative or impact evaluations. In one case, the Population Research Center Program, the program staff at the National Institute of Child Health and Human Development (NICHD) considered undertaking an impact evaluation. They obtained funding through the Office of Evaluation in the Office of the Director of NIH, worked closely with the program evaluation staff in the office of the NICHD director, compared notes with center program staff in other institutes, and consulted with evaluation experts in academia. In the end, they decided on a formative evaluation, because the field is small and therefore selecting centers because they had top researchers (and attracted more top researchers after they obtained the center grant) means that there is no comparison group. Instead, the evaluation group consulted with a wide range of people—in funded centers, potential centers, universities without centers, and other funding organizations—and identified trends and made conclusions in the context of the best strategy for the population research program

(which includes research project grants, training awards, and contracts for large-scale surveys as well as the centers).

The Population Research Center Program evaluation led to substantial changes in the program. It also led to formation of an NIH interest group on evaluation of centers, consisting of evaluation officers of many of the institutes, who meet periodically to discuss how to evaluate center programs. This effort may eventually lead to more formalized evaluation criteria and procedures, but was still in the early stages of development when this report was written. This chapter will therefore describe several attempts at evaluation that have been carried out by individual institutes, detail some of the obstacles to good evaluations, point out some lessons learned by other agencies in their efforts to conduct similar assessments, and most importantly, propose some general principles and specific measures that ought to be incorporated into future center programs to make evaluation easier and more effective.

PREVIOUS EVALUATIONS OF CENTER PROGRAMS

As noted above, some NIH institutes have conducted evaluations of one or more of their center programs. The committee reviewed 11 such evaluations (see Box 5-1), summaries of which are provided in Appendix F. It is unlikely that these are the only ones that have been carried out, but these 11 were readily available on institute websites and share enough common features that the committee considers them representative.[1] All were conducted, or commissioned by, the institute's national advisory council, which has statutory responsibility for reviewing and approving all research awards made by the institute. The circumstances that generated the evaluations of center programs by institutes varied, but all were ad hoc efforts. That is, they were not a result of a regular preplanned process for periodic evaluation of the center program in question. Many were apparently initiated in response to a perception on the part of the institute direc-

[1]In some cases, evaluations leading to major program changes were not available on the institute website at the time this report was written, for example, the May 2000 report of the Midstream Evaluation Committee for the Comprehensive Sickle Cell Centers cited in the RFA for Comprehensive Sickle Cell Centers released in December 2000 (RFA-HL-01-015) and the February 2003 expert panel review of the Botanical Research Centers Program cited in the most recent RFA for this program in December 2003 (RFA-OD-04-002), now posted at http://nccam.nih.gov/training/centers/bot-research-index.htm. It should also be noted that the National Center for Research Resources (NCRR) has conducted formal evaluations of some of its programs, including the Research Centers in Minority Institutions Program, which was evaluated in 2000 by an outside evaluation firm under the supervision of an expert advisory panel of extramural scientists (NCRR, 2000b).

BOX 5-1
Some Previous NIH Evaluations of Specific Center Programs

National Cancer Institute

- Institute of Medicine, 1989. A Stronger Cancer Centers Program: Report of a Study.
- Cancer Centers Program Review Group, 1996. Report to the Director.
- Ad Hoc P30/50 Working Group, 2003. Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future.

National Institute of Arthritis and Musculoskeletal Diseases

- Centers Working Group II, 1997. Summary Report to the Institute Director.

National Institute of Deafness and Communication Disorders

- Work Group on Single and Multiple Project Grants, 1998. Report to the Director.

Office of Aids Research

- Focus Group to Review the Centers for AIDS Research (CFAR) Program, 1999. Report to the Director.

National Institute of Child Health and Human Development

- Demographic and Behavioral Sciences Branch, 1999. Report of the Demographic and Behavioral Sciences Branch Population Centers Review.

National Heart, Lung, and Blood Institute

- Committee to Redefine the Specialized Centers of Research Programs, 2001. Report of the Committee to Redefine the Specialized Centers of Research Programs.

National Institute on Aging

- National Institute on Aging, 2002. Report of the Alzheimer's Disease Centers External Advisory Meeting.

National Institute of Nursing Research

- National Advisory Council for Nursing Research, 2002. Minutes of the Advisory Council Meeting of May 21-22, 2002.

National Center for Complementary and Alternative Medicine

- Research Centers Program Expert Panel, 2002. Research Centers Program Expert Panel Review.

tor or staff, or one or more advisory council members, that the program was not accomplishing the goals originally set out for it or that developments in the field merited a review of the continued relevance of a long-standing program. Few of the reports contained data measuring outputs or impacts of centers (some recommended that the program staff collect data that could be used to evaluate the program in the future), and they relied heavily on testimony of center directors. In most cases the authors began with the assumption that there was a continuing need for a center program in some form. The relative paucity of external evaluations, given the number of center programs and center awards, reflects the difficulty in evaluating center programs. The following section describes some of the reasons for this.

CHALLENGES IN EVALUATION OF CENTER PROGRAMS

The program evaluations noted in Box 5-1 and summarized in Appendix F were all carried out by groups of highly reputable individuals, predominantly accomplished scientists, written up in a formal report, and posted on an institute website. Despite the shortcomings and limitations of the reports listed in the previous section, the committee commends the authors for taking on the task of evaluation at all. Given the resources and data available to them for the task, the reports probably represent the state of the art. The following sections suggest some reasons why this is the case.

Results Take a Long Time

The initial project period for most center grants is most often five years, a period that is long enough for competent scientists with good ideas to produce some papers for peer-reviewed publications. This is especially true in the case of core grants, which provide a richer infrastructure for scientists who already have their own research project grants. Centers will generally take a little longer to get organized and running than an individual laboratory, however, and center programs often start with only a few centers and build up the number of centers over several years, which makes it difficult to fully evaluate the program, as distinguished from individual centers, after the first five years. Also, in the case of disease-focused centers, the primary goal is to help move basic science discoveries into clinical research and practical applications. Clinical research is an increasingly highly regulated endeavor that depends heavily on the availability and cooperation of patient-subjects, which reduces the speed with which the research can be accomplished. Impact on health care takes far longer. In a recent paper, Balas and Boren (2000) calculated the time between publication of nine

landmark trials of new clinical procedures and a utilization rate of 50 percent as 15.6 years.

Centers Are More than Center Grants

Center products, publications included, are often the result of a combination of activities at a center, only some of which are supported by the center grant. The most obvious case is that of the core support grants, which aim to facilitate independently funded research by center-affiliated investigators. Certainly a center whose affiliated scientists had no publications would be deemed a failure, as would a core center program whose centers could point to no publications after five years. It is more difficult to draw a conclusion about a core center whose investigators publish frequently or in high-prestige journals, or both. How much credit should go to the center? The individual investigators would very likely have published with or without the center, which was intended primarily as a cost-effective way to provide common resources to a group of investigators. The question, which is difficult to answer, is, did publications come faster than they would have without the center award or are they more interdisciplinary or translational than they would have been in the absence of a center?

Several center program evaluations cited the fact that the centers in question had succeeded in attracting additional research and infrastructure support from other institutes, agencies, foundations, and industry, as well as from their own parent institution. All those sources of support no doubt claim the very same publications and outcomes of center activities as results of their largesse.

Centers Do Several Things at Once

Specialized (P50) and comprehensive (P60) centers are often charged with far more than supporting a program of research at their institution. Centers of Excellence in Cancer Communications Research, for example, are expected to support three or more individual research projects that reflect hypothesis-driven research, plus pilot or developmental research projects, shared resources (cores), and career development. They are also expected to develop mechanisms for dissemination of research findings and products, and foster formal and informal intercenter collaborations. Cooperative Centers for Translational Research on Human Immunology and Biodefense are to have at least five components: (1) assay, reagent, and technology development; (2) three or more research projects; (3) core facilities to support research and manage the center; (4) short-term pilot projects; and (5) an education component focused on short-term training. Each center in such a program tends to be a unique combination of the desired

elements. Trying to add them up to a result for the program tends to underemphasize what may be most important about each center. Evaluation then must be multifaceted as well and must include some decision rules about what to do about centers that do only some of their tasks, but do them extremely well, and centers that do all their tasks but none of them remarkably well.

Human Resources Are Hard to Track

A commonly cited benefit of centers is that they are fertile grounds for training researchers and thereby expand the pool of scientists working in the area of interest. Some programs require some educational or training component; others permit it; still others expect that it will take place even though no funding is provided for it. Like health impacts, however, results of this training take a long time to emerge. The trainees, whether predoctoral or postdoctoral, clinicians, junior faculty exploring a research career, or senior researchers switching the focus of their work, tend to move around in pursuing their careers, and following them for any length of time after they leave the center would require a substantial investment.

Much of the Value Added by Centers Is Intangible

Infrastructure is hard to measure. Providing services and resources used by many investigators on a centralized basis seems like an obvious way to increase efficiency, but demonstrating the savings or the increased productivity of the investigators is a daunting task. Research is by its nature unpredictable, advances often come in spurts, and the needs of investigators vary with the results of their experiments. As a result, simple before-and-after comparisons may be misleading.

Other benefits of centers can be even harder to measure. A very common reason given for starting center programs is a perceived need for multidisciplinary collaboration. Centers are seen as a way to attract established scientists from many disciplines to a common problem area and a common locale, where their increased interaction will promote the desired interdisciplinary studies. Measures of such interaction are conceivable but are likely to be time consuming and expensive. Collaborations can be indexed more easily, by looking at the authors of publications from the center, but it would be much harder to establish that these collaborations result from the existence of a center.

Even more difficult to measure is the oft-cited "synergy" that ideally makes a center more than the sum of its parts, the sense of teamwork that many feel emerges at a successful center, and the culture of collaboration that follows. Social scientists can operationalize and measure these con-

cepts, but there are currently no standard, easy-to-use, or inexpensive instruments.

Peer Reviewers May Be Beneficiaries of the Program

Given the lack of data on outcomes and impacts, evaluation of center programs, like that of any research program, must rely substantially on expert judgment (National Academy of Sciences, National Academy of Engineering, Institute of Medicine, 2001). Ideally, the peers doing the review, whether it is a review of a proposal in a study section or an institute's special emphasis panel, a site visit in connection with a grant renewal, or a program evaluation, should be among the leaders in the relevant field. This can be difficult to arrange in any of these instances, and evaluation of centers brings added difficulties. For example, established centers may loom so large in their field that it is difficult to find experts for external evaluation panels without conflicts of interest. The potential reviewers of the center program may all be leading scientists in individual centers or be affiliated with an institution that is the recipient of a center award. In the case of new center programs trying to implement a new research thrust (moving discoveries about disease etiology toward new diagnostics or treatments, for example), the most knowledgeable scientists in the field may themselves be applicants or strongly biased in favor of the older approach that has brought them success to date.

LESSONS FROM OTHER AGENGIES

The Government Performance and Results Act (GPRA) has produced heightened interest in assessing research in all its forms, not just at NIH but among all the federal agencies that fund research. Some general lessons on research program evaluation were provided by a National Academies report that analyzed how federal agencies that support science and engineering research were responding to GPRA (National Academy of Sciences, National Academy of Engineering, Institute of Medicine, 2001). The report panel examined the responses of the National Science Foundation (NSF), NIH, Department of Defense, Department of Energy, and National Aeronautics and Space Administration. Most of the report's recommendations are GPRA-specific, but three are potentially applicable to any assessment of a research program. The panel recommended that (1) federal research programs, both basic and applied, be reviewed regularly; (2) the primary method of assessment be expert review for quality, relevance, and leadership; and (3) agencies work toward greater transparency and clear validation of methods.

Several agencies' struggles with the problem of assessing research pro-

grams antedate GPRA, however, including some efforts focused directly on centers. The efforts of NSF are particularly instructive.

National Science Foundation

NSF currently supports nearly 300 centers in a wide variety of center programs.[2] They fall into two broad areas: (1) centers focused on scientific problems too complex, too long-term, or too expensive for individual investigator grants, or that require cross-disciplinary collaboration, and (2) centers aimed at the transition of scientific and engineering research into usable solutions for national problems. NSF sees both types of centers as playing a key role in furthering the advancement of science and engineering in the United States, particularly through their encouragement of interdisciplinary research and the integration of research and education. The goals these centers share in common are similar to the goals for many of the NIH-funded centers:

- To address scientific and engineering questions with a long-term, coordinated research effort by involving a number of scientists and engineers working together on fundamental research addressing the many facets of long-term complex problems;
- To include a strong educational component that establishes a team-based, cross-disciplinary research and education culture to educate the nation's next generation of scientists and engineers to be leaders in academe, industry, and government; and
- To develop partnerships with industry that help to ensure that research and education are relevant to national needs and that knowledge migrates into innovations in the private sector.

In the 1980s NSF launched several large center programs—Science and Technology Centers (STCs) and Engineering Research Centers (ERCs)—that substantially increased its investment in centers (from 3 percent of the research budget in 1980 to 7 percent in 1990). In January 1992 NSF's program evaluation staff convened a workshop to devise and sharpen methods for evaluating outcomes of research center programs. Four working groups were formed and asked to focus on outcomes and measures of impact in research, education, technology/knowledge transfer, and institutional impact, respectively. McCullough (1992) summarized the principal questions for measurement in each of the four areas as follows:

[2]http://www.nsf.gov/bfa/bud/fy2003/ideas.htm.

- Research

Do centers develop new perspectives that reflect the organized character and collaborations they encourage? (Are they actually studying distinctively different kinds of problems that are more complex, broader, or longer-term?)

Are problems formulated in novel ways; does research move in directions it otherwise could not have? (Do the centers fill a special niche in their research field?)

- Education

Do the "learners," be they students, faculty, or industrial partners, acquire the insights and competencies necessary to perpetuate the scientific field?

To what degree are learners bringing practical benefits to the university or industry they work in or to the intellectual environment of the center itself?

- Knowledge/Technology Transfer

How is the program designed to make an impact, and who is the customer?

What is industry getting from the centers that it could not get from individual investigators?

What is the evidence that the centralized, multidisciplinary structure of centers makes university/industry collaboration more efficient?

- Institutional Impact

What organizational or policy changes occurred in the parent institutions as a result of creating centers?

What broader changes (e.g., in the culture of research) can be attributed to a program of centers or to the funding of center programs generally?

A number of cautions were offered for would-be evaluators. These included:

- As outcomes to be measured are made more and more specific, and hence more easily measured, they also become less generalizable to other centers and center programs. A common collection of outcome measures might be possible but the elements might have to be weighted differently depending on the program being evaluated.
- Data collection is a sensitive issue, not only because of time and cost, but because in many instances, program directors may already be

demanding considerable data from the centers. Every effort should be made to inventory existing data for suitability.

- In measuring impacts (as opposed to outcomes), isolating the effects of the center programs will be quite difficult.
- A thorough and systematic evaluation of center program outcomes will take time and money.

The STC program had grown to 25 university-based centers by 1995 and was in the eighth year of a planned 11-year lifetime when the Committee on Science, Engineering, and Public Policy (COSEPUP) of the National Academies was asked to help with the decision about whether this experimental program should be continued and, if so, in what form. Specifically, COSEPUP was to review and interpret a body of data previously gathered by an outside contractor, Abt Associates (Fitzsimmons et al., 1996), draw its own conclusions about the program's progress toward its goals, and make recommendations for the future use of the STC mode of support. The study was not to critique individual centers, but to evaluate the program as a whole.

The COSEPUP panel concluded that NSF and the nation were receiving a good return on a relatively small investment. It found that "most STCs were producing high quality research that would not have been possible without a center structure, and were a model for the creative interaction of scientists, engineers, and students in various disciplines and across academic, industry, and other institutional boundaries" (National Academy of Sciences, National Academy of Engineering, Institute of Medicine, 1996). The COSEPUP panel's conclusion was not based on empirical data collected by Abt Associates, which were based on potentially biased self-reports from individuals who were direct or indirect beneficiaries of a center. COSEPUP's own conclusions about the STC program relied heavily on reports of site visits, which were conducted annually by committees of experts for the first three years of each center's existence, at 18-month intervals thereafter, and in conjunction with three-year and six-year renewal competitions.

The ERC program has undergone several systematic reviews. ERCs annually collect and report data on several performance outputs, such as number of publications, student enrollments, patents, and interactions with industrial partners. These data, along with site visits by external reviewers, are used by NSF in periodic reviews used to determine continued funding and midcourse changes, as needed, in research priorities and administrative arrangements. Program reviews of selected aspects of the ERC program have also been conducted by external consultants. Among these reviews have been survey-based assessments of the impacts of ERCs on the performance of ERC-based graduate students in their initial post-ERC jobs (Abt

Associates, 1996) and the characteristics of ERC interactions with their industrial partners (Ailes et al., 1997).[3] The plans of ERCs to maintain their activities following the expiration of NSF support were also the subject of an external review (Ailes et al., 2000).

POSSIBLE METHODOLOGIES

One attractive approach to evaluation is systematic comparison of center awards with other types research support in order to determine the "value added" by use of the center mechanism. Staff located a 1989 study that used such a strategy to look at the funding mechanisms supporting 13 major advances in cancer research (Narin, 1989). Narin used citation analysis to identify the key research papers in 13 major advances in cancer research and used the acknowledgment of support in each paper to link it to National Cancer Institute (NCI) support mechanisms, namely, R01, P01, R10 (now U10), P30, contract, and intramural. An obvious flaw in this approach is one noted above—the cancer centers supported by P30 core grants do not fund research directly, but rather support investigators with R01 grants and other sources of support. Therefore publications of scientists working in NIH-supported cancer centers might acknowledge the R01 grant that funded the research, but not P30 facilities and services that also contributed. Nevertheless, although Narin's analysis showed that R01 and P01 grants and the NCI intramural program were acknowledged most frequently as a source of support by the key papers that were among the highly cited in their field (top 10 percent), P30 support was acknowledged by a majority of the highly cited papers.

Committee member Myron Weisfeldt recounted an unpublished comparison of center grants and multiproject P01 grants in which he participated as a member of the NHLBI's Cardiology Advisory Committee in the late 1980s. The study compared NHLBI's Specialized Centers of Research Excellence in Acute Myocardial Infarction to P01-supported research on the same topic. Evidence for impacts was sought in three realms: scientific, investigator development, and human health. In the first of these, evidence was bibliographic; investigator development was assessed in terms of electees to the American College of University Cardiologists, and human health impact was reduction of the one-year mortality from acute myocardial infarction. The study concluded that center grants and multiproject P01 grants produced roughly similar publication records, but that centers had far greater impacts on training future academic cardiologists and in reducing the mortality rate. It should be noted, however, that P01 grants

[3]These two studies have been synthesized by Parker (1997).

rarely have a training component although graduate students and postdoctoral fellows receive valuable research experience. It is also unlikely that many of the P01 grants had an explicitly clinical focus.

Other examples might be adduced to recommend comparison studies as the evaluation method of choice, but the committee believes that these two illustrate pitfalls that lie in that path. Instead, it recommends that evaluation take the form of a comparison of results achieved versus the expressed goals of the program. These goals will vary widely, corresponding to the wide variety of center programs that exist at NIH. A simple one-size-fits-all evaluation template will therefore not be feasible, but the remainder of this section contains some possible measures and methods that could be incorporated into a program-specific evaluation plan.

Indicators

Under this heading the committee includes numerous, often quantitative, measures of center program activities. Sometimes, but not always, they are generated in the course of program or center operations and therefore do not impose a major additional burden on either center or program staff. These indicators may in some instances be products (outputs) of those activities; in other cases they may be only descriptions, listings, or counts of activities taking place at the centers or taking place elsewhere in response to center activities (processes); in still other cases they may merely be descriptions of resources provided to or obtained by the centers (inputs) to make those activities possible.

Impacts on health are the most desirable indicators, but as noted above, some of the most important indicators of the impact of successful medical research, namely reductions in mortality and morbidity, may not become apparent for many years, and separating out the impact of specific mechanisms is extremely difficult. In the interim, intermediate outputs can be identified, for example, number of publications in the scientific literature and citation rates. In addition to outputs, program evaluation frequently relies on inputs and program activities as surrogate measures of long-delayed outcomes. At the center level these measures might include the number of new grants received or increases in the level of university support, the number of new scientists recruited and students trained, the number of interdisciplinary conferences held, and the number of projects under way. At the program level, one might point to changes in medical school curricula, changes in national policies and treatment guidelines, and utilization rates for new or altered interventions. Inputs, for example, dollars spent or number of centers established, are the indicators of last resort, or they are used only in evaluations taking place very early in the life of a program.

Box 5-2 contains a list of the types of indicators that institutes might

BOX 5-2
Potential Indicators for Evaluating NIH Center Programs

Goal:	Increased basic and clinical research in program's area of focus.
Indicators:	Increased number of studies in each category being funded, especially new studies; increased number and impact of publications and presentations of center research.
Goal:	More multidisciplinary research.
Indicators:	Increased number of collaborations established; increased number and percent of center studies, especially center scientific publications authored by teams of scientists from two or more university departments; greater number of disciplines represented among center-affiliated staff.
Goal:	More translational research.
Indicators:	Increased number of publications in clinically oriented journals; patent applications; licenses issued; and clinical trials under way or completed.
Goal:	Increased or more effective support, or both, for independently funded investigators.
Indicators:	Larger number of studies supported, especially new studies; more types and amounts of support supplied; characteristics of core facilities, materials and services available; increased number of publications of center-affiliated investigators.
Goal:	Increased attention to program's area of focus by centers' home institutions, scientific community, and general public.
Indicators:	Increased institutional support for center operations (space, faculty and staff, recognition on institutional organizational charts and publications); additional research funding from NIH and other public agencies, nonprofit organizations, and commercial industry.
Goal:	Successful recruitment of established researchers to the program's area of interest.
Indicators:	More scientists with previous publications in the area joining the center; increased number of new grants or other funding obtained by these new investigators; number of publications, patents, or other products of work at the centers.
Goal:	Development of new investigators.
Indicators:	More trainees associated with the programs' centers; current positions of former trainees; research grants subsequently won by these trainees at program centers or elsewhere; larger number of trainees who are elected members or fellows of professional societies.

continued

BOX 5-1 Continued

Goal:	Expanded education of health professionals.
Indicators:	Increased number of courses, seminars, and workshops offered by program centers; larger number of health professionals attending.
Goal:	Expanded education of the general public.
Indicators:	Increased number of publications in the popular press, radio or television appearances by center staffs, increases in patient load for relevant health problems; increased percentage of patients agreeing to participate in clinical research.
Goal:	Demonstration of state-of-the-art prevention, diagnosis, and treatment techniques.
Indicators:	Increased number of seminars, grand rounds, workshops, and other educational programs conducted; larger number of local and regional practitioners participating in such programs.

consider in evaluating their programs of center awards. The list is intended to be suggestive rather than all-inclusive, and in recognition of the varying goals of center programs, it is organized by some of the most commonly expressed goals of current center programs. Collection and analysis of data on the indicators should be included in the program design, and the awards should require centers to provide specific data for program evaluation as well as monitoring purposes.

Site Visits, Interviews, and User Surveys

Statistical indicators, whether collected en passant or specifically for purposes of program evaluation, are by their nature limited to quantifiable goals. Nearly every program evaluation combines these indicators with first-hand observations or other site-specific efforts to gather relevant information. Given the prominence in descriptions of centers of such intangibles as synergy and facilitation, any assessment of a center program should strongly consider inclusion of site visits to centers; interviews with center staff and other members of the institutions in which the centers are embedded; and systematic mail or phone surveys of program and center staff and, especially in the case of center infrastructure or core grants, systematic mail or phone surveys of the independent investigators whom the centers were designed to support.

Designing Evaluation into Center Programs

NIH has established an extensive set of procedures for evaluating center applications for initial and renewal funding (although the use of site visits has been declining for budgetary reasons), and program officers review annual progress reports from centers. Some institutes have adopted sunset provisions for individual centers (i.e., no more than two five-year grants) or, in one case, conduct site visits in the third year of a center's five-year award to assess whether to encourage a renewal proposal for a second award. Also, both initial and renewal applications are competitive, and poorly performing centers can be, and are, replaced individually.

Most center *programs* are not subject to the same level of periodic scrutiny as individual centers are when they apply for renewal (competitive continuations). Where there are regular program reviews by an institute's national advisory council, they generally encompass a major program unit, e.g., the three program divisions of the National Institute of Allergy and Infectious Diseases and the six program divisions of the National Institute on Aging, in which a center program is just one of many activities. Renewal RFAs and PAs are not always reviewed as intensively or at the same level of review (i.e., by a chartered external advisory committee) as they were when they were new program initiatives. Formal evaluation plans are not usually developed at the beginning of a center program, so the data that will be needed in five or more years will be identified and collected from the start of the program.

Finding. NIH does not have formal regular procedures or criteria for evaluating center programs. From time to time, institutes conduct internal program reviews or appoint external review panels, but these ad hoc assessments are usually done in response to a perception that the program is no longer effective or appropriate rather than part of a regular evaluation process. Most of these reviews rely on the judgment of experts rather than systematically collected objective data, although some formal program evaluations have been performed by outside firms using such data.

Recommendation 5. Every center program should be given a formal external retrospective review for its continued effectiveness on a regular basis (at least every five to seven years). The review should be coordinated at an organizational level above the centers program itself.

a) The review should be performed by people at arms-length distance from the program and with the appropriate expertise to judge the varied activities of the centers. The views of interested publics, including the scientific and advocacy communities, as well as NIH officials and grantees, should be solicited as a matter of course.

b) The program should be evaluated against its original objectives and with regard to contemporary challenges in its field. The review should include consideration of the question, "Are centers still the most appropriate means of making progress in this field?" and the criteria should be consistent with those adopted or developed in response to Recommendation 3 for establishing the center program in the first place.

c) The review should use multiple sources of evidence to evaluate the effectiveness of the program, and its conclusions should be evidence-based. The review might consider, for example, the scientific impact (e.g., publication counts and impacts, important discoveries, development and sharing of research tools); impact on human health (e.g., changes in health status); and impact on human resources (e.g., career paths of pre- and postdoctoral students and investigators).

d) A program evaluation plan should be developed as part of the design and implementation of new center programs, and data on indicators used in the evaluation plan should be collected regularly and systematically. Data should be collected from the centers according to a common format. Many of the indicators should also be useful for program monitoring and progress reporting. One set of potential indicators is provided in Box 5-2.

e) Each institute's plan for evaluating center programs should be linked to its strategic planning process.

REFERENCES

Abt Associates. 1996. *Job Performance of Graduate Engineers Who Participated in the NSF Engineering Research Centers Program*. Report to the National Science Foundation, NSF Contract END 94-13151. Bethesda, MD: Abt Associates.

Ailes C, Roessner D, Feller I. 1997. *The Impact on Industry of Interaction with Engineering Research Centers*. Final report prepared for the National Science Foundation. Arlington, VA: SRI International.

Ailes C, Roessner D, Coward J. 2000. *Documenting Graduation Paths: 2nd Year Report to the National Science Foundation*. Arlington, VA: SRI International.

Balas EA, Boren SA. 2000. Managing clinical knowledge for health care improvement. In: Bemmel J, McCray AT, eds. *Yearbook of Medical Informatics 2000: Patient-Centered Systems*. Stuttgart, Germany: Schattauer Verlagsgesellschaft. Pp. 65-70.

Fitzsimmons SJ, Grad O, Lal B. 1996. *An Evaluation of the NSF (National Science Foundation) Science and Technology Centers (STC) Program*. Cambridge, MA: Abt Associates. Vol. I: Summary.

Lenfant C. 2002. Strengthening commitment to clinical research: The National Heart, Lung, and Blood Institute's Specialized Centers of Research program. *Circulation* 105(4):400-401. [Online]. Available: http://www.nhlbi..nih.gov/funding/fromdir/circ-1-02.htm [accessed December 15, 2003].

McCullough J. 1992. *Draft Report of the NSF/Program Evaluation Staff Workshop on Methods for Evaluating Programs of Research Centers, January 1992*. Washington, DC: National Science Foundation.

Narin F. 1989. The impact of different modes of research funding. In: Ciba Foundation Conference. *The Evaluation of Scientific Research*. Chichester, England: John Wiley & Sons. Pp. 120-140.

National Academy of Sciences, National Academy of Engineering, Institute of Medicine. 1996. *An Assessment of the National Science Foundation's Science and Technology Centers Program*. Washington, DC: National Academy Press.

National Academy of Sciences, National Academy of Engineering, Institute of Medicine. 2001. *Implementing the Government Performance and Results Act for Research, A Status Report*. Washington, DC: National Academy Press.

NCRR (National Center for Research Resources). 2000. *Evaluation of the Research Centers in Minority Institutions Program: Final Report 2000*. Bethesda, MD: National Center for Research Resources.

Parker L. 1997. *The Engineering Research Centers (ERC) Program: An Assessment of Benefits and Outcomes*. Arlington, VA: National Science Foundation. [Online]. Available: http://www.nsf.gov/pubs/1998/nsf9840/nsf 9840.htm [accessed December 15, 2003].

6

Closing Comments and Thoughts About the Future

Section 7 of Public Law 107-84, the MD-CARE Act (Muscular Dystrophy Community Assistance, Research and Education Amendments of 2001), called on the Secretary of Health and Human Services to enter into a contract with the Institute of Medicine for the purpose of conducting a study and making recommendations on the impact of, need for, and other issues associated with extramural center programs funded by the National Institutes of Health (NIH). It further specified six major areas that were to be considered in conducting the study. This report is organized around those six areas, but reflecting the committee's views of their relative importance, not all are addressed in a chapter or section of their own. The executive summary provides a précis of the report. Rather than repeat that summary here, the remainder of this chapter addresses each of the six congressional concerns in turn, offers a brief summary of the committee's findings, and refers the reader to the part or parts of the report containing more detail.

1. *The current areas of research incorporating Centers of Excellence (which shall include a description of such areas) and the relationship of this form of funding mechanism to other forms of funding for research grants, including investigator-initiated research, contracts, and other types of research support awards.*

Chapter 2 is primarily devoted to description and data on the current status of NIH center programs. Center grants have constituted less than 10

percent of the NIH budget each year for more than a decade. In February 2003 NIH reported that it was funding 1,209 research center grants at an annual cost of $2.4 billion. Center programs and the centers vary greatly in size, purpose, and organization, reflecting in part different strategies among the NIH institutes and differences among research areas in the state of the science, amount of infrastructure needed for cutting edge research, and nature and burden of the health problem addressed. NIH funds these center programs in a wide variety of ways as well, but there appear to be several broad types of NIH center awards. In the committee's terms, these are:

- *Center Infrastructure* awards, or core grants, which fund a director, core services (administrative and technical), and shared facilities and equipment to focus research on a particular set of questions and to support a group of investigators whose research is funded by independently obtained research project grants.
- *Research Center* awards, which fund not only shared services but research projects as well. In some cases, they may also support additional activities, such as community education, screening, and counseling programs, and education of medical and allied health professionals about state-of-the-art diagnostic, prevention, and treatment techniques.
- *Research Resource Center* awards, which fund centers to develop and provide research resources and tools to researchers across the country (examples include nonhuman primate centers, mutant mouse and other animal resource centers, islet cell resource centers, proteomics centers, and microbial genome sequencing centers).

Centers of Excellence can be found in all three categories. The committee therefore elected to address center programs as a group rather than attempt to generalize about only those center programs using the term "centers of excellence" in their title. NIH envisions these programs, which can be funded by cooperative agreements or contracts as well as by grants, as complementing the investigator-initiated grants that make up the major portion of the research portfolios of the institutes. More information on the interdigitation of different types of award mechanisms is provided in the following section on distinctive aspects of centers, but some extramural scientists argue that these institute-initiated and institute-reviewed center programs are at odds with the highly decentralized initiation and highly centralized review processes that have been central to NIH's success. The committee believes that both approaches have their roles.

2. *The distinctive aspects of Centers of Excellence, including the additional knowledge that may be expected to be gained through Centers of Excellence as compared to other forms of grant or contract mechanisms.*

It should be noted that centers are extramural entities located in a university or an independent research institution. The activities of centers may be supported by many sources in addition to an NIH center grant, and centers typically undertake many activities beyond those required by the terms of their NIH center grant (providing care for patients, for example, paid for by the patients or their insurance). In fact, designation as a center frequently facilitates the conduct of those other activities in a way that leads supporters to describe their center as something greater than the sum of its parts. With that in mind, examination of center program documents published by NIH between January 1, 2001, and March 1, 2003, led to the following synthesis of the major justifications offered for centers or center programs:

- Centers enable a stable, long-term institutional focus on a complex set of problems that cross disciplinary lines, which is difficult to foster through traditional investigator-initiated grants to individual investigators.
- Centers can provide a locus for patient-oriented clinical, behavioral, and epidemiological research that typically has not fared well in the discovery-oriented system for review of investigator-initiated research proposals but is necessary for translation of fundamental knowledge into clinical advances.
- By making expensive resources accessible, centers can enhance quality, facilitate productivity, and promote the cost-effectiveness of other externally supported investigator-initiated research projects.
- Designation as an NIH-supported research center confers distinction on the area of research and thus helps attract additional competitive funding from private as well as public sources, facilitates fundraising, increases the interest and support of medical school leaders and colleagues, and supplies a valuable incentive in recruiting new faculty, staff, and trainees.
- Centers in academic medical centers can be important means of facilitating the transfer of clinical research results into community practice by developing and then demonstrating the latest techniques.
- A network of similar centers can combine their resources to ask questions that no one institution could address alone. The most obvious case is that of large clinical trials, where such a network can take advantage of a greatly expanded patient pool to conduct the trial faster and more efficiently than would be possible in any single site.
- Center awards are a way to build the infrastructure to promote the institutional development of a field of research (e.g., nursing, population research), develop research capacity at minority-serving institutions or in-

stitutions in regions with little NIH research funding, and build research infrastructure to respond to public health emergencies.

Many of these points, which are drawn from Chapter 2, are revisited and documented with a number of examples in Chapter 4, where the criteria for initiating a center program are addressed.

3. The costs associated with establishing and maintaining Centers of Excellence, and the record of scholarship and training resulting from such centers. The research and training contributions of centers should be assessed on their own merits and in comparison with other forms of research support.

The costs of center programs are documented in Chapter 2. In February 2003, when NIH submitted its fiscal year (FY) 2004 budget request to Congress, it estimated it would fund 1,209 research center awards in FY2003 at a cost of $2.4 billion. Funding for center grants has generally increased in line with the overall NIH budget in recent years, constituting between 8.5 percent and 9 percent of all NIH funding during the 1992 to 2003 period. In FY2002 the average center award was $1.7 million per year. Not surprisingly, given the wide variety of center types, the range spanned three orders of magnitude, from $55 thousand to $56 million per year (the median center grant was $1.3 million per year). To put these costs in perspective, the mean value of the most common individual project award, the R01, was approximately $326,000 per year in FY2002.

The record of scholarship and training produced by centers is much more difficult to document. Each institute evaluates the individual centers it funds on a case-by-case basis as the centers apply for renewal awards, but few systematic studies of the center programs themselves have been done. The wide variety of centers is one barrier to sweeping generalizations, but in large measure the difficulty is a consequence of the fact noted above that centers typically draw funding from many sources and undertake many activities not specifically mandated by the NIH center award they hold. In the simplest case, centers supported by what NIH calls core grants use the funds to facilitate the work of independently funded scientists at their institution by providing space, shared services and equipment, and the like. The research itself is funded by other grants from NIH (and often other sources as well). Under such circumstances, sorting out credit for the resulting scholarship is extremely difficult. In addition, center program managers and the peer reviewers who judge renewal applications regularly attempt to sort out the poorly performing individual centers in a program based on their records of scholarship and training relative to other competing centers.

Center programs themselves are seldom analyzed so closely. Comparison of center program achievements with those other forms of research funding has seldom been attempted and will always be problematic because the various forms of funding are employed for different purposes. The committee believes that evaluations of any of the funding mechanisms should be aimed at assessing the degree to which they have met their specific goals. Chapter 5 describes the barriers to evaluation in more detail, recommends a well-designed, periodic program evaluation of all center programs, and offers some guidance for planning and implementing those evaluations.

4. *Specific areas of research in which Centers of Excellence may be useful, needed, or underused, as well as areas of research in which Centers of Excellence may not be helpful.*

Each of the NIH institutes relies on input from a wide variety of sources in determining when a centers program is appropriate, and no one body of observers, including the present committee, is qualified to predict areas of research that would qualify as unique, unexplored opportunities for all center programs. The process and criteria suggested by the committee in Chapters 3 and 4 for initiation of center programs should be the guides in all cases. This committee notes the recently expressed intent of NIH Director Elias Zerhouni to focus more attention on fostering multidisciplinary team approaches to increasingly complex research questions and on accelerating translation of basic science to clinical research and applications, both of them sets of activities in which centers are likely to be useful mechanisms. Ideally, this expanded use of centers would not come at the expense of investigator-initiated grants, which have stood the test of time as a mechanism for new and junior investigators with innovative ideas to reach professional maturity.

5. *Criteria that may be applied in determining when Centers of Excellence are an appropriate and cost-effective research investment and conditions that should be present in order to consider the establishment of Centers of Excellence.*

Chapters 3 and 4 discuss the initiation and adoption of center programs in detail, and Table 4-1 provides criteria for initiating both infrastructure and research center programs. In brief, the criteria focus on the importance of the problem to be addressed by the program, need for shared resources, need to develop a highly visible critical mass of multidisciplinary research, number of researchers working in the field, need for strategic

focus, need for interdisciplinary interaction, need for translation of scientific knowledge into clinical or public health practice, and existence of a body of clinical questions in need of scientific research.

6. *Alternative research models that may accomplish results similar to or greater than Centers of Excellence.*

NIH currently employs a number of mechanisms that could be alternatives to centers for fostering and supporting interdisciplinary research, translational research, collaborations among researchers in different places, and shared research resources. In addition, there are or could be alternatives within the center model itself. Chapter 2 describes many of these alternatives, which include the program project (P01) grant to support a small group of investigators conducting research with a common theme, Interactive Research Project Grants, in which related R01 research project grants are submitted together, and mini core grants, in which R24 (or U24) research resource-related grants are used to encourage already-funded investigators to work together on a problem by providing resources not available where investigators are working separately. For clinical research, especially clinical trials, where direct interactions between basic researchers and clinical investigators for translational research purposes are not called for, but coordinated activities by multiple clinical centers are needed, NIH often uses cooperative agreements (e.g., U10, U01, and U19 awards) or contracts.

The center model itself has been evolving from a problem-focused organizational structure that cuts across disciplinary department lines within a research institution to an independent component of a network involved in multicenter collaborative as well as center-specific research. Another alternative has been to use existing centers rather than create new ones for a specific disease or other problem. Some emerging research opportunities or health emergencies are met by providing supplements to centers. In another case, centers for research on fragile X syndrome were located at existing centers for research on mental retardation and are, in effect, components of the mental retardation centers.

NIH has also been experimenting with Web-based virtual laboratories, also called collaboratories. The National Center for Research Resources (NCRR) has funded seven collaboratories through supplemental awards to some of its existing biotechnology resource centers (NCRR, 2000, 2002). One of these, the Biomedical Informatics Research Network, is developing the network, data-storage, and software tools needed for geographically separated investigators conducting research involving neuroimaging to share

and use large sets of data on brain images from the molecular scale to the whole brain.

The committee discussed some additional alternatives. One would be to allow individual investigators to apply for support of center projects whose form and structure are designed by the applicant rather than specified in a Program Announcement, Request for Applications, or institute guidelines. This could lead to centers organized differently or addressing problems differently (or different types of problems) than those solicited by NIH. It might encourage collaborative translation, clinical, and population projects that investigators believe are too risky or novel to submit to study sections more oriented toward basic science projects. Another committee alternative would be to broaden initiatives to reduce health disparities to encourage partnerships between centers in research-intensive institutions and rural health facilities. The Alzheimer's Disease Centers supported by the National Institute of Allergy and Infectious Diseases, for example, are affiliated with satellite diagnostic and treatment clinics that recruit minority, rural, and other underserved patients to increase the diversity of study volunteers.

THE FUTURE OF CENTER PROGRAMS

Center programs are a small but important element in NIH's array of responses to its dual mission of pursuing fundamental knowledge about the nature and behavior of living systems and bridging the gap between basic science discoveries and developing better ways to apply that knowledge to extend healthy life and reduce the burdens of illness and disability. For all but four institutes, center programs currently consume less than 10 percent of each institute's budget. All institutes employ the center mechanism, typically after extensive consultative and review procedures, to promote research and activities that are not well-suited for support through the bellwether investigator-initiated awards that are the hallmark of publicly funded biomedical science in the United States. Some centers simply focus on making the work of independently funded investigators more efficient, but others, including the disease-oriented centers frequently suggested by Congress, also provide support for multidisciplinary research and other activities aimed at turning important scientific discoveries into clinically useful applications. There is general agreement in the scientific community that the center mechanism has been particularly successful in that sphere. One institute director described the role of centers this way:

> Continuation of the SCOR [specialized centers of research] program is essential if we are to fulfill our mission as a health-oriented organization. The SCOR is virtually the only mechanism we have available to focus multidisciplinary talent on clinical problems. As the basic science commu-

> nity relies on the program project mechanism, so the clinically oriented community needs the SCOR if it is to move patient-oriented research to the limits of its frontiers (Lenfant, 2002).

More general evidence for the important role played by NIH extramural research centers in supporting clinical research was provided by the NIH Director's Panel on Clinical Research (NIH, 1997), which concluded that center programs were the *only* NIH research mechanism predominantly dedicated to the full spectrum of clinical research. The panel's data are now more than six years old, but current NIH award data show that there has been a continuation of the same proportion of overall funding dedicated to clinical research.[1] This present committee believes that centers continue to be leading performers of research that links basic science discoveries with applications in the clinical sciences.

The proportion of extramural awards devoted to such institute-initiated center programs has not changed appreciably in the last decade (one of this committee's recommendations, however, is that NIH revamp its current system for counting and tracking centers to ensure that all center awards are classified as such). Assessments like those expressed above by National Heart, Lung, and Blood Institute Director Claude Lenfant and in the following quote from the National Cancer Advisory Board's Ad Hoc P30/P50 Working Group suggest that substantial segments of the biomedical research community as well as NIH officials see the centers mechanism as an important, indeed essential, component of NIH's portfolio of funding mechanisms:

> The P30/P50 Working Group believes that the P30 centers program should be a centerpiece of the nation's cancer research investment. The stability and centralized support provided through this funding mechanism allow institutions to conduct a wide array of investigations into the etiology and treatment of cancers. At a time when clinical research is increasingly expensive and difficult to conduct, cancer center support is especially critical in ensuring that there are places where cutting-edge basic, clinical, prevention and control, as well as translational cancer research can be conducted. Cancer centers serve as an essential setting for clinical investigations by providing the critical links between the bench and the bedside (NCAB, 2003).

Moreover, judging from the pronouncements of a number of leaders in the field, including the present director of NIH, support for centers and similar mechanisms might well grow significantly over the next decade. Eric Lander, director of the Whitehead Institute Center for Genomic Research

[1]The most recent estimate of clinical research funded by NIH is $8.4 billion in FY2003 (Zerhouni, 2003b).

and one of the leaders of the International Genome Sequencing Consortium, recently offered his view that biology is in the midst of a transition from trying to discover important individual components and molecules to trying to discover how the pieces fit together and function. He stressed that these integrative projects are going to require collaborative efforts that transcend what can be accomplished in a single lab (Metheny, 2003).

The Association of American Medical Colleges, Association of American Universities, and National Association of State Universities and Land-Grant Colleges, together representing the nation's medical schools, teaching hospitals, leading research universities, and public institutions of higher learning, recently offered answers to several questions posed by the NCRR that resonate with Lander's views (Cohen et al., 2003). In response to a question about the most important research trends in biomedical research, they cited the:

- Increasing complexity and sophistication of biomedical research. Much of this research relies on advanced technologies, informatics, and other emerging tools, as well as on shared research resources that often require dedicated professional staff.
- Growth in multi- and cross-disciplinary research, the emergence of new disciplines, and the growing need for investigative teams with diverse and specialized skills and capabilities.
- Accelerating translation of basic science to clinical research and applications (and vice versa). Moreover, the horizons of clinical research now extend to public health and health security, the needs of underserved communities, and other areas well beyond the traditional clinical environment.

NIH Director Elias Zerhouni voiced a very similar theme in his opening statement to the House Subcommittee on Labor-Health and Human Services-Education Appropriations for the FY2004 Presidents Budget Request (Zerhouni, 2003a). He summarized the results of a series of meetings he had convened to develop a roadmap for NIH, defined as a short list of initiatives that would make the biggest impact on biomedical research. The meetings, which included leading extramural scientists as well as NIH institute directors, resulted in three major themes:

1. *New pathways to scientific discovery*. For example, vital information about the proteins that make up the human body, molecular libraries, nanotechnology, computational biology and bioinformatics, and molecular imaging.
2. *Changing dynamics of the research teams of the future*. Because of the complexity and scope of today's scientific problems, traditional mentor-

apprentice models must be replaced by integrated teams of specialists from numerous disciplines that were considered unrelated in the past. Imaging research, for example, requires cell biologists, computer programmers, radiologists, and physicists to work collaboratively on new diagnostics and treatments.

3. *Need to reengineer the national clinical research enterprise for optimal translation of our discoveries into clinical reality*. This means supporting multidisciplinary clinical research training career paths, introducing innovations in trial design, stimulating translational research, building clinical resources like tissue banks, developing large clinical research networks, and reducing regulatory hurdles. It includes a standard clinical research informatics strategy that will permit the formation of nationwide communities of clinical researchers made up of academic researchers, qualified community physicians, and patient groups.

Zerhouni concluded his summary by pointing out that these three thematic areas focus on technologies and systems that will enable researchers of the future to not only solve problems more quickly, but also to ask questions that we have not been able to ask before—questions so complex that without the aid of these efforts, they would be impossible to address.

Whether or not one agrees with Zerhouni's vision of the road ahead in biomedical research, or that center programs will be, or ought to be, key vehicles for the trip, it seems apparent that center programs are not likely to diminish in number or importance in the near future. At least two of the three Roadmap themes—fostering integrated research teams and organizing for translational research—have been driving forces behind the establishment of center programs in the past.[2] Whether they will continue to be effective in the future, however, will depend on addressing a number of

[2]On September 30, 2003, after this report was drafted, NIH made public the initiatives it is planning to implement the Roadmap for Medical Research (Zerhouni, 2003b). As expected, new center programs will play a prominent role in implementing the Roadmap objectives. In September and October 2003, NIH issued eight Requests for Applications (RFAs) under the Roadmap, five of them for new center programs. They include: National Centers for Biomedical Computing (U54); National Technology Centers for Networks and Pathways (U54); Exploratory Centers for Interdisciplinary Research (P20); Development of High Resolution Probes for Cellular Imaging (P20); and Centers for Innovation in Membrane Protein Production (P50). At least three more center programs are planned: Nanomedicine Centers, Bioactive Small Molecule Library and Screening Centers, and Regional Translational Research Centers. Funding over six years is planned to be $2.1 billion, or $350 million a year on average, although funding in the first year (FY2004) will be approximately $128 million (Kaiser, 2003). According to the five center RFAs, up to $45 million has been set aside for center awards in FY2004.

potential obstacles that have not yet been resolved. Some of the issues that require careful thought in considering the appropriate role of center programs in the future include:

- The amount of funds available for new biomedical research supported by the NIH. NIH budget growth is not likely to match the experience of the past five years of near 15 percent annual increases. In the worst case—growth at less than the rate of inflation—the expansion of centers in number or size, or both, would require a redistribution of funding among mechanisms.
- The importance of expanding the translational aspect of linking basic science funding with clinical research is one of the main justifications of the center mechanism, but it is not apparent that the critical mass of clinical investigators that will be needed to conduct the necessary research is available or now in training. Moreover, the current demands on clinical faculty for patient care and teaching and the academic requirements for promotion and tenure discourage young physician-investigators from entering a research track as a career.
- Historically, the goal of teaching and training of young scientists for the doctorate has been to prepare them to conduct an independent research program. Although industry frequently states that it needs investigators trained to work in teams, the current method of evaluating the educational and research accomplishments of students in training is antithetical to producing scientists with experience in team research.
- Current academic recruiting, promotion, and tenure policies are based on individual accomplishment. The inability or reluctance of those who make those decisions to expand their criteria to include contributions to a multidisciplinary team of researchers presents a formidable challenge to expansion of center programs and other team-based large-scale biomedical science (IOM and NRC, 2003).
- The accommodation in academia of larger and more effective centers carries with it the problems of dedicated space, long-term academic appointments, and administrative issues that must be reconciled with current department-oriented activities. This issue is of importance when considering a policy of sunsetting center programs.

In sum, greater emphasis on use of the center mechanism for support of biomedical research will require careful long-term planning and restructuring of many long-held academic traditions.

REFERENCES

Cohen J, Hasselmo N, Magrath P. 2003. "National Center for Research Resources 2004 Strategic Plan, 68 FR 4503-4." Letter from the presidents of the Association of American Medical Colleges, Association of American Universities, and National Association of State Universities and Land-Grant Colleges to the National Center for Research Resources (NCRR) in response to NCRR's call for comments on its draft strategic plan. [Online]. Available: http://www.aau.edu/research/Ltr5.9.03.pdf [accessed December 15, 2003].

IOM and NRC (Institute of Medicine and National Research Council). 2003. *Large-Scale Biomedical Science: Exploring Strategies for Future Research*. Washington, DC: The National Academies Press.

Kaiser J. 2003. Speeding up delivery: NIH aims top push for clinical results [News]. *Science* 2003(5642):28-29.

Lenfant C. 2002. Strengthening commitment to clinical research: The National Heart, Lung, and Blood Institute's Specialized Centers of Research program. *Circulation* 105(4):400-401. [Online]. Available: http://www.nhlbi..nih.gov/funding/fromdir/circ-1-02.htm [accessed December 15, 2003].

Metheny B. 2003. Science training must embrace teamwork, collaboration, preparation for work outside academia, thought leaders say. *Washington Fax*, May 13.

NCAB (National Cancer Advisory Board). 2003. *Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future*. Report of the National Cancer Advisory Board Ad Hoc P30/P50 Working Group. [Online]. Available: http://deainfo.nci.nih.gov/ADVISORY/ncab/p30-p50/P30-P50final12feb03.pdf [accessed December 15, 2003].

NCRR (National Center for Research Resources). 2000. *NCRR Biomedical Collaboratories Workshop Report*. [Online]. Available: http://www.ncrr.nih.gov/biotech/btcollab wrkshprpt10-2000.pdf [accessed December 15, 2003].

NCRR. 2002. *Data and Collaboratories in the Biomedical Research Community*. [Online]. Available: http://www.ncrr.nih.gov/biotech/collabmtg2002.asp [accessed December 15, 2003].

NIH (National Institutes of Health). 1997. *Report from the Director's Panel on Clinical Research to the Advisory Committee to the Director* [of NIH]. [Online]. Available: http://www.nih.gov/news/crp/97report/index.htm [accessed December 15, 2003].

Zerhouni E. 2003a. Opening Statement on the FY2004 President's Budget Request, "FY 2004 Appropriations Overview," Hearing before the House Appropriations Subcommittee on Labor, Health and Human Services, and Education, April 2, 2003. [Online]. Available: http://www.nih.gov/about/director/budgetrequest/FY2004budgetrequest.htm [accessed December 15, 2003].

Zerhouni E. 2003b. The NIH Roadmap (Policy Forum). *Science* 302(5642):63-64,72. [Online.] Available: http://www.sciencemag.org/cgi/content/full/302/5642/63?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=zerhouni%2C+e&searchid=1069347433605_6563&stored_search=&FIRSTINDEX=0&fdate=10/1/2003&tdate=11/30/2003 [accessed October 3, 2003].

A

NIH Center Programs

NCI

- Cancer Research Centers (P30/P20)
- Specialized Programs of Research Excellence (SPOREs) in Human Cancer (P50)
- In Vivo Cellular and Molecular Imaging Centers (P50)
- Transdisciplinary Tobacco Use Research Centers (P50)
- Comprehensive Minority Institution/Cancer Center Partnerships (U54/U56/P20)
- Centers of Excellence in Interventions Directed at Molecular Targets (U54) (also called Interdisciplinary Research Teams for Molecular Target Assessment)
- Clinical and Epidemiologic Centers in the Early Detection Research Network (U01)
- Biology-Chemistry Centers (P01)
- Small Animal Imaging Resource Programs (R24)
- Centers of Excellence in Cancer Communication Research (P50)
- Network for Translational Research: Optical Imaging (U54)
- *Integrative Cancer Biology Programs/Teams (P50/P20)

NOTE: Programs marked with an asterisk (*) were new and had not made any awards as of November 1, 2003.

NEI

- Core Grants for Vision Research (P30)
- Vision Research Infrastructure Development Grants (R24)

NHGRI

- Large-Scale Human Genome Sequencing Centers (U54)
- Large-Scale Genotyping Centers for the Haplotype Map of the Human Genome (U54)
- Centers of Excellence in Genomic Science (P50) (cosponsor: NIMH)
- Biotechnology Centers (P41)
- Center for Inherited Disease Research (contract)
- Encyclopedia of DNA Elements (ENCODE) Research Network (U01/U19/U41)
- *Centers for Excellence in Ethical, Legal, and Social Implications Research (P50/P20)

NHLBI

- Specialized Centers of Research (SCORs) (P50)
- Specialized Centers of Clinically Oriented Research (SCCORs) (P50) (replacing the SCORs, above)
- Centers for Reducing Asthma Disparities (U01)
- Comprehensive Sickle Cell Centers (P60)
- Proteomics Centers (contract)
- DNA Re-sequencing and Genotyping Program (contract)
- Cardiovascular Disease Enhanced Dissemination and Utilization Centers (contract)
- Center for Fetal Monkey Gene Transfer for Heart, Lung, and Blood (U01)

NIA

- Alzheimer's Disease Centers (P30/P50)
- Edward R. Roybal Centers for Translational Research in the Behavioral and Social Sciences (P30)
- Claude D. Pepper Older Americans Independence Centers (P30/P60)
- Nathan Shock Centers for Excellence in Basic Biology of Aging (P30)
- Resource Centers for Minority Aging Research (P30)
- Centers on the Demography of Aging (P30)

NIAAA

- National Alcohol Research Centers (P50/P60)

NIAID

- Autoimmunity Centers of Excellence (U19)
- Centers for Prevention of Autoimmune Diseases (U19)
- Asthma and Allergic Diseases Research Centers (P01)
- Cooperative Centers for Translational Research on Human Immunology and Biodefense (U19/R21)
- Centers for AIDS Research (P30) and Developmental Centers for AIDS Research (P20)
- Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (U54/U56)
- *Biodefense Proteomics Centers (contract)
- *Bioinformatics Resource Centers for Biodefense and Emerging/Reemerging Infectious Diseases (contract)
- Human Immunology Centers of Excellence (P01)
- Vaccine Immunology Basic Research Centers (P01)
- Tropical Medicine Research Centers (P50)
- Hepatitis C Cooperative Research Centers (U01/U19)
- Sexually Transmitted Infections and Topical Microbicides Cooperative Research Centers (U19)
- Chronic Fatigue Syndrome Cooperative Research Centers (U19)
- International Centers for Excellence in Research (R03)
- *Microbial Genome Sequencing Centers (contract)
- Malaria Research and Reference Reagent Resource Center (contract)
- Tuberculosis Prevention Research Center (contract)
- Pathogen Functional Genomics Resource Center (contract)

NIAMS

- Multipurpose Arthritis and Musculoskeletal Diseases Centers (P60)
- Multidisciplinary Clinical Research Centers for Arthritis and Musculoskeletal and Skin Diseases (P60) (replacing the P60 Multipurpose Arthritis and Musculoskeletal Diseases Centers, above)
- Skin Diseases Research Core Centers (P30)
- Rheumatic Diseases Core Centers (P30)
- Musculoskeletal Disorders Core Centers (P30)
- SCORs (P50)
- Muscular Dystrophy Cooperative Research Centers (U54/R21) (cosponsors: NICHD, NINDS)

NICHD

- Cooperative Contraceptive Research Centers (U54)
- Population Research Infrastructure Program (R24/R21) (replaced Population Research P30 Centers Program)
- Specialized Cooperative Centers Program in Reproduction Research (U54)
- Cooperative Reproductive Science Research Centers at Minority Institutions (U54)
- Cooperative Specialized Infertility Research Centers (U54)
- Learning Disabilities Multidisciplinary Research Centers (P50)
- Child Health Research Centers (P30)
- Mental Retardation and Developmental Disabilities Research Centers Program (P30)
- Fragile X Research Centers (P30)

NIDA

- Transdisciplinary Prevention Research Centers (P50/P20)
- P50 centers
- Centers for the Development of Medications to Treat Drug Dependence (P50) (also called Medication Development Units)
- Centers for Drug Abuse and AIDS Research (P30)
- Treatment Research Centers (P60)
- *NIDA Neuroproteomics Research Centers (P30)

NIDCD

- Research Core Center Grants (P30)
- Clinical Research Center Grants (P50)

NIDCR

- Comprehensive Oral Health Research Centers of Discovery (P60)
- *Specialized Centers for Oral, Dental and Craniofacial Research (P50) (replacing the P60 Comprehensive Oral Health Research Centers of Discovery)
- Centers for Research to Reduce Oral Health Disparities (U54)

NIDDK

- Diabetes Research and Training Centers (P60)
- Diabetes Endocrinology Research Centers (P30)

- Diabetes Centers of Excellence (P01)
- Molecular (formerly Gene) Therapy Centers (P30)
- Cystic Fibrosis Research Centers (P30)
- Specialized Centers for Cystic Fibrosis Research (P50)
- George M. O'Brien Urologic Research Centers (P50)
- George M. O'Brien Kidney Research Centers (P50)
- Centers of Excellence in Pediatric Nephrology (P50)
- Interdisciplinary Centers for Polycystic Kidney Disease Research (P50)
- Centers of Excellence in Molecular Hematology (P30)
- Clinical Nutrition Research Units (P30)
- Obesity/Nutrition Research Centers (P30)
- Silvio O. Conte Digestive Diseases Research Core Center Grants (P30)
- Digestive Diseases Research Development Centers (R24)
- Inflammatory Bowel Disease Genetics Research Centers (U01)
- Mouse Metabolic Phenotyping Centers for Models of Diabetes and Its Complications (U24)
- NIDDK Biotechnology Centers (U24)

NIEHS

- Environmental Health Sciences Core Center Grants Program (P30)
- Marine and Freshwater Biomedical Centers (P30)
- Centers for Children's Environmental Health and Disease Prevention Research (P01) (cosponsors: EPA, CDC)
- Comparative Mouse Genomics Centers Consortium (U01)
- National Center for Toxicogenomics Proteomics Resource (contract)
- National Center for Toxicogenomics Microarray Resource (contract)
- Collaborative Centers for Parkinson's Disease Environmental Research Consortium Program (U54)
- Breast Cancer and the Environment Research Centers (U01) (cosponsor: NCI)
- *Centers for Oceans and Human Health (P50) (with NSF)
- Centers for Population Health and Health Disparities (P50) (cosponsors: NCI, NIA, OBSSR)

NIGMS

- Centers of Excellence in Complex Biomedical Systems Research (P50/P20)

- Centers of Excellence in Chemical Methodologies and Library Development (P50)
- Centers for Structural Genomics (P50)
- Research Centers in Trauma, Burn, and Perioperative Injury (P50)
- Exploratory Center Grants for Human Embryonic Stem Cell Research (P20)
- Large-Scale Collaborative Project Awards ("Large Glue Grants") (U54/R24)
- Protein Structure Initiative (U54)
- Biotechnology Centers (P41)
- Native American Research Centers for Health (S06) (cosponsor: Indian Health Service)

NIMH

- Autism Research Centers of Excellence (U54 and R21) (cosponsors: NICHD, NINDS, NIDCD, NIEHS)
- Advanced Centers for Interventions and Services Research (P30) and Developing Centers for Interventions and Services Research (P20) (consolidation of 4 center programs: Social Work Research Development Centers, Prevention Research Centers, Specialized Mental Health Interventions Research Centers, Centers for Research on Services for People with Mental Health Disorders)
- *Developing Research Centers on Interventions for the Prevention of Suicide (P20) (cosponsors: NIDA, NIAAA)
- Translational Research Centers in Behavioral Science (P50)
- Interdisciplinary Behavioral Science Centers for Mental Health (P50)
- Core Grants for Enhancing Neuroscience Translation (R24)
- Silvio O. Conte Centers for Neuroscience Research (P50)
- Silvio O. Conte Centers for the Neuroscience of Mental Disorders (P50)
- Silvio O. Conte Centers to Develop Collaborative Neuroscience Research (P20)
- Centers Program for Research on HIV/AIDS and Mental Health (P30)
- Research Core Centers for Advanced Neuroinformatics Research (P30)
- Mouse Neuroscience Phenotyping and Distributing Center (contract)
- Center for Collaborative Genetic Studies on Mental Disorders (R24)

NINDS

- Morris K. Udall Parkinson's Disease Research Centers of Excellence (P50) (cosponsor: NIEHS)
- P50 centers on brain injury and stroke, epilepsy, multiple sclerosis, narcolepsy, spinal cord injury, etc.
- Specialized Neuroscience Research Programs at Minority Institutions (U54) (cosponsors: NCMHD, NCRR, NIMH)
- Institutional Center Core Grants to Support Neuroscience Research (P30)
- Specialized Programs of Translational Research in Acute Stroke (P50)
- Microarray Centers for Research on the Nervous System (U24) (cosponsor: NIMH)
- NINDS Cooperative Program in Translational Research (U54/U01/U13)
- *National Centers for Neurofibromatosis Research (P50) (cosponsor: NIDCD)

NINR

- Nursing Research Centers (P30/P20)
- Nursing Partnership Centers on Health Disparities (P20) (cosponsor: NCMHD)

NCCAM

- Centers of Excellence for Research on Complementary and Alternative Medicine (P01)
- Developmental Centers for Research on Complementary and Alternative Medicine (U19)
- Planning Grants for International Centers for Research on Complementary and Alternative Medicine (R21) (cosponsor: FIC)
- Centers for Complementary and Alternative Medicine Research (P50) (cosponsors: NCI, NHLBI) (being phased out and replaced by the three programs listed above)
- Exploratory Program Grants for Frontier Medicine Research (P20)

NCMHD

- Research Infrastructure in Minority Institutions (RIMI) Program (P20)

- Project EXPORT: Centers of Excellence (Excellence in Partnerships for Community Outreach, Research on Disparities in Health, and Training) (P60/P20/R24)

NCRR

- General Clinical Research Centers (M01)
- Clinical Research Resources (U42), including:
  - National Gene Vector Laboratories (cosponsors: NCI, NIDDK, NIAMS, NINDS)
  - Human Pancreatic Islet Cell Resource Centers (cosponsors: NIDDK, Juvenile Diabetes Research Foundation International)
- Biomedical Technology Resource Centers (P41), including:
  - Biomedical Informatics Research Network (BIRN)
- National Primate Research Centers (P51)
- Animal Research/Comparative Medicine Centers (P40/U42)
- Research Centers in Minority Institutions (RCMI) (G12)
- Centers of Clinical Research Excellence at NCRR-Supported RCMIs (U54/P20)
- Comprehensive Centers on Health Disparities at RCMI Eligible-Institutions (U54)
- Centers of Biomedical Research Excellence (COBRE) (P20)
- Biomedical Research Infrastructure Network (BRIN) (P20)
- Rare Disease Clinical Research Network (U01) (cosponsors: ORD, NINDS, NICHD, NIAMS, NIDDK)
- *High Throughput Genotyping Centers for Human and Animal DNA (U54) (cosponsor: NCI)
- *Exploratory Centers for Interdisciplinary Research (P20)
- *National Technology Centers for Networks and Pathways (U54)
- *National Centers for Biomedical Computing (U54)

OFFICE OF THE NIH DIRECTOR

- Botanical Research Centers (P50/P01) (Office of Dietary Supplements, with cosponsors NCCAM, NIEHS)
- Centers for Mind/Body Interactions and Health (P50) (Office of Behavioral and Social Science Research, with cosponsors NCI, NHLBI, NIA, NIAAA, NIAMS, NICHD, NIDCR, NIDA, NIGMS, NIMH, NINDS, NINR)
- Specialized Centers of Research on Sex and Gender Factors Affect-

ing Women's Health (P50) (Office of Research on Women's Health, with cosponsors NIAMS, NICHD, NIDDK, NIDA, NIEHS, NIMH, and FDA)

- Planning Grants: National Programs of Excellence in Biomedical Computing (Pre-NPEBC) (P20) (cosponsors: NCI, NIBIB, NIGMS, NHLBI, NIMH, NCRR, NLM)

B

Biographical Sketches of Committee and Staff

RONALD W. ESTABROOK, Ph.D., (*Chair*) is Virginia Lazenby O'Hara Professor of Biochemistry at the University of Texas Southwestern Medical School. In his 14-year tenure as Chairman of the Biochemistry Department, he built a world-recognized center of biochemical research, in particular, research related to the cytochrome P450s. In addition Dr. Estabrook served as the first Dean of the Graduate School of Biomedical Sciences at the Dallas campus of the University of Texas. In 1990 Dr. Estabrook was named the occupant of the Cecil and Ida Green Chair in the Biomedical Sciences at the University of Texas Southwestern Medical Center at Dallas. After undergraduate education at Rensselaer Polytechnic Institute, Dr. Estabrook did his graduate training in biochemistry at the University of Rochester, after which he took a postdoctoral position in biophysics to work with Britton Chance at the University of Pennsylvania. After three years of research on mitochondrial cytochromes, he traveled to England to study at the Molteno Institute, Cambridge University, with David Kielin (the discoverer of cytochromes). Dr. Estabrook subsequently joined the faculty of the School of Medicine of the University of Pennsylvania, where he advanced to the rank of Professor of Physical Biochemistry. It was during this time, in the early 1960s, that Dr. Estabrook, together with Drs. David Cooper and Otto Rosenthal of the Department of Surgery of the University of Pennsylvania, discovered the enzymatic (functional) properties of the hemoprotein, now known as cytochrome P450. Since 1982 Dr. Estabrook has been applying the techniques of molecular biology to the

study of the enzymatic properties of different P450s expressed in different types of cells and, with his colleagues in Dallas, potential commercial application of P450 enzymes to major problems of chemical synthesis, drug discovery, and the biomodification of organic systems. Dr. Estabrook has coauthored more than 260 publications, including editing 14 books. He has received many honors, including election to the Institute of Medicine of the National Academy of Sciences in 1975, election to the National Academy of Sciences in 1979, and an honorary Doctor of Medicine degree from the Karolinska Institut in Stockholm, Sweden, in 1981, and a Doctor of Science from the University of Rochester (1981). He has served on numerous national and international advisory committees including the Governing Board of the National Research Council of the National Academy of Sciences and the Council of the Institute of Medicine of the National Academy of Sciences.

SUSAN E. COZZENS, Ph.D., is Professor and Chair of the School of Public Policy at the Georgia Institute of Technology. Her current research is on science, technology, and inequalities, and she is active internationally in developing methods for research assessment and science and technology indicators. From 1995 through 1997, Dr. Cozzens was Director of the Office of Policy Support at the National Science Foundation (NSF). The Office coordinated policy and management initiatives for the NSF Director, primarily in peer review, strategic planning, and assessment. Dr. Cozzens has served as a consultant to the Committee on Science, Engineering, and Public Policy of the National Research Council, Office of Science and Technology Policy, NSF, Institute of Medicine, Office of Technology Assessment, General Accounting Office, National Cancer Institute, National Institute on Aging, the National Institutes of Health, and the National Institute on Occupational Safety and Health, and on advisory committees for the American Association for the Advancement of Science (Liberal Education and the Sciences, EPSCOR Evaluation), the National Academy of Sciences (NSF Decision-making for Major Awards), and the Office of Technology Assessment (Human Genome Project). She has been an invited speaker on science policy and research evaluation at the Ministry for Research and Technology in France, the Research Council of Norway, the Institute for Policy and Management in Beijing, and the Fundamental Science Foundation of Sao Paulo, Brazil, and is incoming chair of the Committee on Science, Engineering, and Public Policy of the American Association for the Advancement of Science. Dr. Cozzens has a distinguished record of publication and service in the fields of science policy and science and technology studies. She is past editor of *Science, Technology, & Human Values*, the journal of the Society for Social Studies of Science, and has served on councils and committees for several professional societies. She is author of

Social Control and Multiple Discovery in Science: The Opiate Receptor Case, and coeditor of *Theories of Science in Society* (with Thomas F. Gieryn); *The Research System in Transition* (with Peter Healey, Arie Rip, and John Ziman); and *Invisible Connections: Instruments, Institutions, and Science* (with Robert Bud). Her work has appeared in *Issues in Science and Technology, Policy Studies, Journal of Technology Transfer, Evaluation, and Program Planning, Neuroscience, Social Studies of Science, Knowledge: Creation, Diffusion, Utilization, Scientometrics, Science and Public Policy*, and *Research Policy*, and she has contributed chapters to a dozen books. She is coeditor of *Research Evaluation*. Her Ph.D. is in sociology from Columbia University (1985) and her bachelor's degree from Michigan State University (1972, summa cum laude). She is a recipient of Rensselaer Polytechnic Institute's Early Career Award, a member of Phi Beta Kappa and Phi Kappa Phi, and a Fellow of the American Association for the Advancement of Science.

IRWIN FELLER, Ph.D., is Senior Visiting Scientist, American Association for the Advancement of Science and Professor Emeritus of Economics, The Pennsylvania State University, where he served on the faculty from 1963-2002 and as Director of the Institute for Policy Research and Evaluation from 1977 to 2002. Dr. Feller's current research interests include the evaluation of federal and state science and technology programs, the economics of academic research, and the university's role in technology-based economic development. He is the author of *Universities and State Governments: A Study in Policy Analysis* and over 100 refereed journal articles, final research reports, and book chapters, as well as of numerous papers presented to academic, professional, and policy audiences. He has been a consultant to the President's Office of Science and Technology Policy; National Aeronautics and Space Administration; Carnegie Commission on Science, Technology, and Government; Ford Foundation; National Science Foundation (NSF); National Institute of Standards and Technology; U.S. General Accounting Office; U.S. Department of Education; U.S. Department of Energy; and several state governments. He has served on National Academies committees on international benchmarking of U.S. science and manufacturing modernization. He formerly chaired the American Association for the Advancement of Science's Committee on Science, Engineering, and Public Policy. Currently, he is chair of NSF's Advisory Committee to the Assistant Director for Social, Behavioral, and Economic Sciences, a member of NSF's Advisory Committee on the Government Performance and Results Act, and a member of the National Research Council's Transportation Research Board's Research and Technology Coordinating Committee.

CHARLES K. FRANCIS, M.D. has served as president of Drew University since 1998. He oversees the University's $60 million budget, the College of Medicine and the College of Allied Health, an extensive research portfolio and numerous community-based research, education, and training programs. Prior to becoming president at Drew, Dr. Francis was a professor of clinical medicine at the College of Physicians and Surgeons of Columbia University and chairman of the department of medicine at Harlem Hospital Center in New York City. A native of Newark, New Jersey, he is a graduate of Dartmouth College and received his medical degree from Jefferson Medical College in Philadelphia. Following an internship at Philadelphia General Hospital, he served as a General Medical Officer in the U.S. Air Force. He received his training in internal medicine and cardiology at Boston City Hospital and Massachusetts General Hospital. Dr. Francis has held posts as clinical instructor and fellow in medicine at Tufts University School of Medicine, and clinical research fellow in cardiology and senior medical resident at Massachusetts General Hospital and Harvard Medical School. Dr. Francis also served as assistant professor of medicine at Drew University, the University of Southern California, and the University of Connecticut School of Medicine, and he served as chief of cardiology at Mount Sinai Hospital in Hartford, Connecticut. Prior to his position at Columbia, he was an associate professor of medicine at Yale University School of Medicine and director of the cardiac catheterization laboratory at Yale-New Haven Hospital. Dr. Francis has contributed to the literature in the areas of coronary artery disease in African Americans, thrombolysis in myocardial infarction, hypertensive heart disease, mitral valve insufficiency, AIDS-associated heart disease, access to medical care, and the advancement of health care of minorities. He has received research support from the National Institutes of Health; the National Heart, Lung, and Blood Institute; and the Harlem Urban Health Research Institute. Dr. Francis is board certified in both internal medicine and cardiology and is a fellow with the American College of Cardiology, the Council on Clinical Cardiology, and the American College of Physicians. He is widely published, serves on several medical journal review boards and is a member of numerous medical professional associations. Dr. Francis currently serves on the Board of Governors of the Warren Magnuson Clinical Center at the National Institutes of Health. He has spent more than 20 years as a volunteer for the American Heart Association (AHA), serving as an affiliate president in Connecticut, on the board of directors in New York, as well as on the national board of directors. He currently chairs the Executive Committee of the AHA Council on Clinical Cardiology, serves on the Woman and Minority Leadership Committee, and sits on the Los Angeles AHA Board of Directors. Dr. Francis is a past recipient of the AHA's Louis B. Russell, Jr., Memorial Award in recognition of his outstanding service to minority and

underserved populations and of the Association of Black Cardiologists' Daniel B. Savage Scientific Achievement Award.

RONALD G. GELLER, Ph.D., joined Health Research Associates as a Senior Associate in October 2002. He received his Ph.D. in 1969 from the University of Wisconsin for his research on cardiovascular physiology. His postdoctoral research at the National Institutes of Health (NIH) focused on urinary kallikrein in animal models and in human subjects and on the pharmacology of peptides of nonmammalian origins, including wasp and hornet venoms. He then held successive positions of ever-increasing responsibilities at NIH. During his 33-year tenure, he participated in virtually every facet of NIH activities. As Chief of the National Heart, Lung, and Blood Institute's (NHLBI's) Hypertension and Kidney Diseases Branch in the 1970s, he managed a research portfolio that included research grants, program projects, centers, contracts, clinical trials, and education research grants. He developed new application and administrative guidelines for the Hypertension Specialized Centers of Research and established collaborative research relationships between centers. As Associate Director for Extramural and Collaborative Programs of the National Eye Institute (NEI) in the 1980s, he promoted the use of cooperative agreements to support multicenter clinical trials and expanded the NEI's use of Core Center Grants and shared resources. While serving as the Director of the Division of Planning and Evaluation in the Office of the NIH Director, he conducted numerous unique analyses that had an impact on NIH policies. During the 1990s, as the Director of the Division of Extramural Affairs in the NHLBI, Dr. Geller managed a staff of more than 100 scientists and other employees whose responsibilities included (1) initial peer review of grants and contracts; (2) grants, management policies, and procedures; (3) contract management; and (4) advisory committee management. The annual extramural budget for NHLBI during this period was about $1 billion. Dr. Geller's most recent NIH position, Director, Office of Extramural Programs, in the Office of the NIH Director, focused on the development and monitoring of policies and procedures that have an impact across NIH. He and his staff performed NIH-wide guidance and oversight for (1) peer review policies, (2) publication of the *NIH Guide for Grants and Contracts*, (3) resolution of issues related to human subjects concerns, (4) research misconduct, (5) research training and career development programs, (6) the Small Business Research programs, (7) the Academic Research Enhancement Award program, and (8) overall extramural staff training.

DAVID G. KAUFMAN, M.D., Ph.D., is Professor and Vice Chair of Pathology and Laboratory Medicine, and Professor of Biochemistry and of Toxicology in the School of Medicine of the University of North Carolina

at Chapel Hill. Following undergraduate study in physics at Reed College, he studied medicine and then obtained a Ph.D. in experimental pathology at Washington University. He pursued residency training in anatomic pathology at Barnes and Washington University Hospitals and did postdoctoral research training at the National Institutes of Health (NIH). He joined the faculty of the University of North Carolina in 1975. Dr. Kaufman's research has focused on endometrial cancer. He participated in studies that confirmed that use of postmenopausal estrogens cause endometrial cancer and demonstrated that therapy with estrogens and progestins combined was protective against endometrial and ovarian cancer. He is a leader in studies of human endometrial cells in culture demonstrating conditions in vitro required to reproduce differentiation as seen in vivo including the formation of glands. He has also developed culture conditions to evaluate epithelial-stromal cell interactions involved in the regulation of structure and function in endometrial tissue and demonstrated that multiple paracrine factors are involved in the mutual signaling between these cells that are needed to achieve homeostasis. Dr. Kaufman served as the president of the Federation of American Societies for Experimental Biology (FASEB) (1999-2000). During his term as president of FASEB he focused on the status of physician scientists in biomedical research and advocated mechanisms to reverse negative trends in physician involvement in research. He is also former president of the American Society for Investigative Pathology, and is a member of the American Association for Cancer Research and the Society of Toxicology. He has served as member and chair of the NIH Chemical Pathology Study Section and was a member of the NCI Cancer Center Support Review Committee. He has also served as member and chair of the American Cancer Society Advisory Committee on Carcinogenesis and Nutrition, and currently sits on their Council for Extramural Grants. He has also served on the Science Advisory Board of the U.S. Environmental Protection Agency, and has been a scientific advisor to the Chemical Industry Institute of Toxicology, the Biology Division of Los Alamos National Laboratory, and the U.S. Department of Energy Low Dose Radiation Research Program. He is presently a member of the Panel on Research of the American Association of Medical Colleges.

J. RICHARD LANDIS, Ph.D., was appointed Director of the Division of Biostatistics, and Vice Chair of the Department of Biostatistics and Epidemiology within the University of Pennsylvania School of Medicine in July 1997. He is Director of the Biostatistics Unit, and Associate Director of the Center for Clinical Epidemiology and Biostatistics (CCEB), an interdisciplinary and interdepartmental research unit. Dr. Landis also directs the Clinical Research Computing Unit (CRCU), a designated core research facility formed to support the conduct of multicenter clinical trials, patient-ori-

ented research projects, and collaborative biostatistical support for clinical research throughout the medical center and the university. He is Professor of Biostatistics within the School of Medicine and holds a secondary appointment as Professor of Statistics in the Wharton School. Dr. Landis earned a B.S. Ed. (1969, magna cum laude) in Mathematics from Millersville University and an M.S. (1973) and a Ph.D. (1975) in Biostatistics from the University of North Carolina at Chapel Hill. He was Professor of Biostatistics at the University of Michigan School of Public Health, where he served on the faculty for 13 years (1975-1988). In 1988, Dr. Landis founded the Center for Biostatistics and Epidemiology at the M.S. Hershey Medical Center of the Pennsylvania State University and served as its director for nine years until 1997, when he relocated to the University of Pennsylvania. His honors include Fulbright Senior Scholar (University of Newcastle, Australia, 1981-1982), Fellow of the American Statistical Association, elected member of the International Statistical Institute, recipient of the Mortimer Spiegelman Gold Medal Award (1984), and recipient of an Environmental Protection Agency Scientific and Technical Achievement Award (1987). He recently finished a term as Associate Editor for *Biometrics*, is a member of the Board of Trustees of the National Institute of Statistical Sciences, and is Chair of the Statistics Section of the American Public Health Association.

STEPHEN MCCONNELL, Ph.D., is Vice President, Advocacy and Public Policy at the Alzheimer's Association. McConnell joined the Association in 1989, and in his career there has led its advocacy and care programs. McConnell is a board member of Citizens for Long-Term Care, a national coalition devoted to raising awareness of the need for a comprehensive solution to long-term care financing. McConnell spent seven years working in the U.S. Congress. From 1984 to 1987, he was staff director of the U.S. Senate Special Committee on Aging under the chairmanship of Senator John Heinz. Earlier, he served as a professional staff member for the U.S. House of Representatives, Select Committee on Aging, under the chairmanship of Representative Claude Pepper. Before moving to Washington, D.C., in 1980, McConnell held a research associate appointment in the Andrus Gerontology Center of the University of Southern California. He has directed major research projects on aging and aging policy, including older worker employment, federal health and housing policy, and the cultural aspects of growing older. McConnell has taught and written on gerontology and social policy. He holds a Ph.D. in sociology from the University of Southern California.

RUTH MCCORKLE, Ph.D., FAAN, is Professor and Director of the Center for Excellence in Chronic Illness Care at the Yale University School of Nursing (YSN). An international leader in cancer nursing, education, and

cancer control research, Dr. McCorkle has done landmark research on the psychosocial ramification of cancer. She was the first research chair of the Oncology Nursing Society and a charter member of that organization as well as of the International Society of Nurses in Cancer Care and has served on the boards of both groups. Dr. McCorkle has been a member of the study sections of the National Cancer Institute (NCI) and the National Institute of Nursing Research (NINR). As the first nonmedical recipient of an NCI Institutional Research Training Grant, she opened the door for other nonmedical fields to become competitive in securing funding. An extremely well-funded researcher, Dr. McCorkle is the principle investigator of "Nursing's Impact on Quality of Life and Cost Outcomes in Ovarian Patients," a grant funded by NINR. She has published extensively and serves on numerous review panels, editorial boards, and professional boards including the American Psychosocial Oncology Society. She was also a member of the National Academy of Sciences Committee on National Needs for Biomedical and Behavioral Research Personnel. Dr. McCorkle was elected to the American Academy of Nursing in 1979 and to the Institute of Medicine in 1990. She was recognized by the American Nurses Association in 1993 as Nurse Scientist of the Year. Dr. McCorkle joined the faculty of YSN in 1998 to assume leadership of the institution's doctoral program. She is also the founding director of YSN's Center for Excellence in Chronic Illness Care, where she collaborates with faculty at YSN and throughout the University who specialize in cancer, cardiovascular disease, diabetes, and HIV/AIDS.

NICOLA C. PARTRIDGE, Ph.D., is Chair of Physiology and Biophysics, UMDNJ-Robert Wood Johnson Medical School. She was previously at Saint Louis University, where she was Professor of Pharmacological and Physiological Science and Orthopedic Surgery. During her tenure there, from 1985 to 2000, she progressed from Assistant Professor of Pediatrics and Orthopedic Surgery to Professor of Pharmacological and Physiological Science and Orthopedic Surgery. In addition, she was Director of the Cell and Molecular Biology Graduate Training Program. A graduate of the University of Western Australia for both her B.Sc. (Honors) and Ph.D. in Biochemistry, Dr. Partridge subsequently underwent postdoctoral training at the University of Melbourne and at Washington University in St. Louis. She has been continuously independently funded by the National Aeronautics and Space Administration or the National Institutes of Health (NIH) since 1987 and has 83 publications. Her research interests are in the areas of parathyroid hormone regulation of gene transcription and regulation of matrix metalloproteinases in bone and cartilage. She is internationally recognized, and her studies have contributed to the understanding of how parathyroid hormone elicits both catabolic and anabolic effects on bone.

Dr. Partridge has co-chaired a number of scientific and policy meetings, and was co-chair of the 1999 Federation of American Societies of Experimental Biology (FASEB) Consensus Conference on the Physician-Scientist. She has served on the editorial boards of the *Journal of Biological Chemistry*, *Journal of Bone and Mineral Research*, and *Calcified Tissue International*. She has served on a number of NIH study sections, in particular, as a member from 1995 to 1999 of the NIH Oral Biology and Medicine Study Section. Dr. Partridge has also functioned in many capacities for the American Society for Bone and Mineral Research. She is presently Vice President for Science Policy of FASEB.

MICHAEL SAAG, M.D., is professor of medicine and director of the 1917 AIDS Outpatient Clinic at the University of Alabama at Birmingham (UAB). Saag, an internationally renowned AIDS researcher and physician, began the 1917 Clinic, originally named for its street address, in 1988. Today, the clinic, relocated in the Community Care Building on the UAB campus, provides medical and social services to approximately 1,000 patients with HIV/AIDS. Dr. Saag, a respected lecturer and mentor, has taught in the department of medicine's division of infectious diseases since 1992. He also serves as a senior scientist and associate director of clinical care and therapeutics with the Center for AIDS Research at UAB, a post he has held since 1988. Dr. Saag serves as chair of the Infection Control Committee for the VA Medical Center in Birmingham and as a member of the executive committee of the UAB Center for AIDS Research. Among his other numerous UAB committee appointments, he is a member of the Hospital AIDS Committee, the UAB AIDS Education Advisory Committee, and the General Clinical Research Center Scientific Advisory Committee. Among his numerous professional associations, Saag chairs the Cryptococcal Subproject Committee of Mycoses Study Group of the National Institutes of Health (NIH). He is a member of the board of directors of the International AIDS Society-USA and serves on the Program Executive Committee of the organization's Educational Program. He is also a member of the Elizabeth Glaser Pediatric AIDS Foundation Grant Review Committee, the NIH Panel to Define Principles of Therapy of HIV Infection and the executive committee of the Forum for Collaborative HIV Research. Dr. Saag received his bachelor's degree in chemistry from Tulane University in New Orleans and his medical degree from the University of Louisville in Kentucky. He completed his internship, residency, and a postdoctoral fellowship at UAB, joining the faculty in 1984 as an associate professor with the department of medicine.

S. LEONARD SYME, Ph.D., is emeritus Professor of Epidemiology at the University of California at Berkeley. Dr. Syme's research focuses on risk

factors for coronary heart disease. His major interest has been psychosocial risk factors such as job stress, social support, and poverty. Since his retirement in 1993, Dr. Syme has devoted most of his time to the development of interventions to prevent disease and promote health. He currently is Director of the Wellness Guide Project, which attempts to provide useful information for the maintenance of health. Dr. Syme was elected to the Institute of Medicine of the National Academy of Sciences and received the Berkeley Citation for Distinguished Achievement, the Lilienfeld Award for Excellence in Teaching, the California Senate Commendation for Illustrious Record of Accomplishment, and the J.D. Bruce Award for Distinguished Contributions in Preventive Medicine.

MYRON L. WEISFELDT, M.D., is the William Osler Professor of Medicine and Director of the Department of Medicine at the Johns Hopkins University School of Medicine, as well as the Physician-in-Chief of Johns Hopkins Hospital. Prior to assuming these positions, Dr. Weisfeldt was the Chairman of the Department of Medicine and Director of the Medical Service at the Columbia Presbyterian Medical Center in New York City. From 1975 to 1991, he was Director of the Cardiology Division at Johns Hopkins University School of Medicine. As Director, he was involved in research on cardiopulmonary resuscitation and survival from sudden cardiac death, the treatment and management of acute myocardial infarction and acute ischemic syndromes, and age-associated changes in cardiovascular function and response to stress. He was Director of the Johns Hopkins Specialized Center of Research in Ischemic Heart Disease from 1977 to 1991. Dr. Weisfeldt received his undergraduate and medical degrees from Johns Hopkins University. He received research training at the National Institutes of Health. His clinical training was at Columbia Presbyterian Medical Center, and he received cardiology training at the Massachusetts General Hospital. Dr. Weisfeldt formerly was President of the American Heart Association and served on the National Advisory Council of the National Institute on Aging. He is currently a member of the Institute of Medicine, the American Society for Clinical Investigation, the Association of American Physicians, and the Association of Professors of Medicine. He received the Golden Heart Award and the Award of Merit from the American Heart Association.

BOARD ON HEALTH SCIENCES POLICY LIAISON

MICHAEL D. LOCKSHIN, M.D., is the Director of the Barbara Volcker Center for Women and Rheumatic Disease at the Hospital for Special Surgery in New York, New York and Professor of Medicine at the Weill College of Medicine of Cornell University. He received his M.D. from

Harvard Medical School in 1963 and did his clinical training at Bellevue Hospital and Memorial Sloan-Kettering Hospital, followed by a fellowship at Columbia-Presbyterian Medical Center. Dr. Lockshin is board certified in internal medicine and rheumatology and has a special interest in gender and rheumatic disease. Dr. Lockshin was Extramural Director (1989-1994), and then Acting Director (1994-1995), of the National Institutes of Health's National Institute of Arthritis and Musculoskeletal and Skin Disorders. He is the author of more than 180 scientific papers and book chapters.

IOM STAFF

FREDERICK J. MANNING, Ph.D., is a Senior Program Officer in the Institute of Medicine's (IOM's) Board on Health Sciences Policy and study director. In nine years at IOM, he has served as study director for projects addressing a variety of topics including medical isotopes, potential hepatitis drugs, blood safety and availability, rheumatic disease, resource sharing in biomedical research, occupational safety and health, and chemical and biological terrorism. Before joining IOM, Dr. Manning spent 25 years in the U.S. Army Medical Research and Development Command, serving in positions that included Director of Neuropsychiatry at the Walter Reed Army Institute of Research and Chief Research Psychologist for the Army Medical Department. Dr. Manning earned a Ph.D. in psychology from Harvard University in 1970, following undergraduate education at the College of the Holy Cross.

ANDREW POPE, Ph.D., is Director of the Board on Health Sciences Policy at the Institute of Medicine (IOM). With expertise in physiology and biochemistry, his primary interests focus on environmental and occupational influences on human health. Dr. Pope's previous research activities focused on the neuroendocrine and reproductive effects of various environmental substances on food-producing animals. During his tenure at the National Academy of Sciences and since 1989 at the Institute of Medicine, Dr. Pope has directed numerous studies on topics that include injury control, disability prevention, biologic markers, neurotoxicology, indoor allergens, and the enhancement of environmental and occupational health content in medical and nursing school curricula. Most recently, Dr. Pope directed studies on priority-setting processes at the National Institutes of Health, fluid resuscitation practices in combat casualties, and organ procurement and transplantation.

MELVIN WORTH, Jr., M.D., is a scholar-in-residence at the Institute of Medicine (IOM). Dr. Worth completed his surgery residency at New York University-Bellevue in 1961 and remained on that faculty for 18 years. He

founded the Bellevue Trauma Service in 1966 and continued as Director until 1979, when he left to become Director of Surgery at Staten Island University Hospital. He served for 15 years with the New York State Office of Professional Medical Conduct and 8 years as a member of the New York State Hospital Review and Planning Council (for which he was Chair in 1993). He is a fellow of the American College of Surgeons, the American College of Gastroenterology, and the International Society for Surgery, and holds memberships in the American Association for the Surgery of Trauma, the Society for Critical Care Medicine, the Association for Academic Surgery, New York Surgical Society (for which he was President in 1979), and other academic and professional organizations. Dr. Worth retains his appointment at New York University, and is clinical professor of surgery at the State University of New York Downstate (Brooklyn) and the Uniformed Services University of the Health Sciences. Dr. Worth most recently served as an IOM study staff member to the Committee on Fluid Resuscitation for Combat Casualties and is the senior advisor to the Committee on Creating a Vision for Space Medicine During Travel Beyond Earth Orbit.

BENJAMIN N. HAMLIN, B.A., is a Research Assistant at the Institute of Medicine. He received his bachelors in Biology from the College of Wooster in 1993 and a degree in health sciences from the University of Akron in 1996. He then worked as a surgeon's assistant in the fields of vascular, thoracic, and general surgery for several years before joining the National Academies in 2000. As a Research Assistant for the Division on Earth and Life Studies at the National Academies, Ben worked with the Board on Radiation Effects Research on projects studying the health effects of ionizing and non-ionizing radiations on the human body. His work at the Institute of Medicine has included *Testosterone and Aging: Clinical Research Directions, Review of NASA's Longitudinal Study of Astronaut Health, Health Literacy: A Prescription to End Confusion, Improving Medical Education: Enhancing the Behavioral and Social Science Content in Medical School Curricula,* and *NIH Extramural Center Programs: Criteria for Initiation and Evaluation*. Ben is currently pursuing graduate work in the sociomedical sciences. He is also involved with the U.S. Bangladesh Advisory Council, an organization that promotes governmental cooperation between the United States and Bangladesh on matters of trade and health care.

NATASHA S. DICKSON has been a senior project assistant with the National Academies' Institute of Medicine since March 2001. She is a graduate of the John S. Donaldson Technical Institute in Trinidad and Tobago. She gained administrative experience at the University of the West Indies,

St. Augustine and also worked as an advertising sales representative and reporter for the Trinidad Express Newspapers.

CONSULTANT

MICHAEL MCGEARY, a political scientist, is a consultant on federal science, technology, and health policy, funding, organization, and evaluation and has authored a number of articles on those topics. He has served as a consultant to the Institute of Medicine (IOM) and other units of the National Academies (Committee on Science, Engineering, and Public Policy; Board on Life Sciences; Division on Engineering and Physical Sciences; Board on International Scientific Cooperation; Office of Scientific and Engineering Personnel; Committee on National Statistics; and Board on Science, Technology, and Economic Policy); Office of Science and Technology Policy; Association of American Universities; SRI International; Washington Advisory Group; Scientific Committee on Antarctic Research; and the Lasker Foundation. Between 1981 and 1995, he worked at the National Academies, where he directed the staff work for a dozen reports by IOM and other committees, including assessments of the cancer centers program of the National Cancer Institute and the AIDS research program of the National Institutes of Health. He did his graduate work at the Massachusetts Institute of Technology and, prior to going to the National Academies, taught at Wellesley College and worked for the National Academy of Public Administration.

C

NIH Research Award Activity Codes and Their Definitions

Extramural research activities are divided into three main mechanisms: grants, contracts, and cooperative agreements. A mechanism is the type of funding application or transaction used at the National Institutes of Health (NIH). In general, with grants, investigators are responsible for developing the concepts, methods, and approach for a research project. With contracts, the awarding unit of the Department of Health and Human Services is responsible for establishing the detailed requirements. With cooperative agreements, both the awarding unit and the recipient have substantial responsibility. Programs are areas within the funding mechanisms, for example, research, training, fellowships, and cooperative agreements. And activity codes identify categories applied to various funding mechanisms.

The codebook for Information for Management, Planning, Analysis, and Coordination, NIH's information system for its extramural programs, provides short definitions of each activity code that constitute NIH-wide definitions.[1] The definitions for the activity codes for center awards and several other common award types are provided below, with the number of awards funded in fiscal year 2002 in brackets.

[1]The latest version of the codebook can be found at: http://grants1.nih.gov/grants/funding/ac.pdf.

CENTER AWARDS

P30 Center Core Grants [317].

To support shared resources and facilities for categorical research by a number of investigators from different disciplines who provide a multidisciplinary approach to a joint research effort or from the same discipline who focus on a common research problem. The core grant is integrated with the center's component projects or program projects, though funded independently from them. This support, by providing more accessible resources, is expected to assure a greater productivity than from the separate projects and program projects.

P50 Specialized Center [343].

To support any part of the full range of research and development (R&D) from very basic to clinical; may involve ancillary supportive activities such as protracted patient care necessary to the primary research or R&D effort. The spectrum of activities comprises a multidisciplinary attack on a specific disease entity or biomedical problem area. These grants differ from program project grants in that they are usually developed in response to an announcement of the programmatic needs of an Institute or Division and subsequently receive continuous attention from its staff. Centers may also serve as regional or national resources for special research purposes.

P60 Comprehensive Center [49].

To support a multipurpose unit designed to bring into a common focus divergent but related facilities within a given community. It may be based in a university or may involve other locally available resources such as hospitals, computer facilities, regional centers, and primate colonies. It may include specialized centers, program projects, and projects as integral components. Regardless of the facilities available to a program, it usually includes the following objectives: to foster biomedical R&D at both the fundamental and clinical levels; to initiate and expand community education, screening, and counseling programs; and to educate medical and allied health professionals concerning the problems of diagnosis and treatment of a specific disease.

U54 Specialized Center-Cooperative Agreements [80].

[The definition is the same as for the P50 specialized center except the following clause is added to the last sentence: "…with funding component staff helping to identify appropriate priority needs."]

P20 Exploratory Grant [208].

To support planning for new programs, expansion or modification of existing resources, and feasibility studies to explore various approaches to the development of interdisciplinary programs that offer potential solutions to problems of special significance to the mission of the NIH. These exploratory studies may lead to specialized or comprehensive centers.

M01 General Clinical Research Centers Program [90].

An award made to an institution solely for the support of a General Clinical Research Center where scientists conduct studies on a wide range of human diseases using the full spectrum of the biomedical sciences. Costs underwritten by these grant include those for renovation, for operational expenses such as staff salaries, equipment, and supplies, and for hospitalization. A General Clinical Research Center is a discrete unit of research beds separated from the general care wards.

P40/U42 Animal (Mammalian and Nonmammalian) Model, and Animal and Biological Material Resource Grants (P40) and Cooperative agreements (U42) [27/30].

To develop and support animal (mammalian and nonmammalian) models, or animal or biological materials resources available to all qualified investigators without regard to the scientific disciplines or disease orientations of their research activities or specifically directed to a categorical program. Nonmammalian resources include nonmammalian vertebrates, invertebrates, cell systems, and nonbiological systems.

P41/U41 Biotechnology Resource Grants (P41) and Cooperative Agreements (U41) [83/0].

To support biotechnology resources available to all qualified investigators without regard to the scientific disciplines or disease orientations of their research activities or specifically directed to a categorical program area.

P51 Primate Research Center Grants [8].

To support centers which include a multidisciplinary and multicategorical core research program using primate animals and to maintain a large and varied primate colony which is available to affiliated, collaborative, and visiting investigators for basic and applied biomedical research and training.

G12 Research Centers in Minority Institutions [26].

To assist predominantly minority institutions that offer the doctorate in the health professions and/or health-related sciences in strengthening and augmenting their human and physical resources for the conduct of biomedical research.

SELECTED RESEARCH PROJECT AWARDS

R01/U01 Research Project Grants (R01) and Cooperative Agreements (U01) [27,568/1,196].

To support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing his specific interest and competencies.

P01/U19 Research Program Project Grants (P01) and Cooperative Agreements (U19) [993/75].

For the support of a broadly based, multidisciplinary, often long-term research program which has a specific major objective or a basic theme. A program project generally involves the organized efforts of relatively large groups, members of which are conducting research projects designed to elucidate the various aspects or components of this objective. Each research project is usually under the leadership of an established investigator. The grant can provide support for certain basic resources used by these groups in the program, including clinical components, the sharing of which facilitates the total research effort. A program project is directed toward a range of problems having a central research focus, in contrast to the usually narrower thrust of the traditional research project. Each project supported through this mechanism should contribute or be directly related to the common theme of the total research effort. These scientifically meritorious projects should demonstrate an essential element of unity and interdependence, i.e., a system of research activities and projects directed toward a well-defined research program goal.

R24/U24 Resource-Related Research Project Grants (R24) and Cooperative Agreements (U24) [213/57].

To support research projects that will enhance the capability of resources to serve biomedical research.

D

NIH Program Planning Process

The normal National Institutes of Health (NIH) process for setting priorities, in which the initiation of new programs, such as research centers, is considered, is complex (NIH, 2001). It is highly decentralized and mostly involves a bottom-up process within each institute. No two institutes employ exactly the same priority-setting procedures. NIH program planning is driven by the annual federal budget process, however, which imposes some top-down structure and higher-level priorities.

At several points, new initiatives have to be fitted within an overall budget figure for NIH; first, within the total the NIH director decides to submit to the Department of Health and Human Services (DHHS), second, the amount allowed by DHHS in its request to the Office of Management and Budget (OMB), third, within the mark for the President's budget request set by OMB, and fourth, within the final appropriation amounts set by Congress and signed into law by the President. In this process, proposals for new programs, such as extramural research centers, well up from program staff, advisory groups of scientific and medical experts and members of the public, professional and scientific organizations, voluntary health associations (VHAs) and patient groups, and other agencies.

NIH also may be asked or directed to establish centers from above by DHHS, the White House, or, most often, by Congress. If centers are mandated, NIH must establish them regardless of what their priority would have been within the NIH planning system.

The annual federal budget process is the principal driver of the program planning and priority-setting process, resulting in decisions about the

existence and funding of programs. A number of pathways converge to feed into this process beyond internal staff initiatives, however, including the views of constituency groups of many kinds, the Administration, and Congress. The institutes also engage in long-range strategic planning, periodic program reviews, and research agenda-setting exercises, all involving outside advice from standing and ad hoc advisory groups. NIH-wide planning and program collaboration and coordination are less well developed, although the increasing focus of research on complex biological phenomena that cross institute boundaries is resulting in more multi-institute center (and other) programs and more NIH director-level advisory and planning mechanisms. All proposals to establish new programs of centers compete with other new and existing programs for funding in the budget process (unless Congress specifies the amount of funding for a center program in the appropriations process, in which case NIH must accommodate that amount in its budget).

STRATEGIC PLANNING

In 1998 the NIH director asked the institutes to submit five-year strategic plans. This request followed the tenor of an Institute of Medicine (IOM) report, *Scientific Opportunities and Public Needs* (IOM, 1998), which recommended that the NIH director take steps to more systematically identify cross-cutting scientific opportunities and needs and to foster unified or joint programs to address them.[1] Some institutes were already engaged in long-range planning to assist in priority setting, such as the National Eye Institute (NEI), which has produced multiyear plans for vision research since 1975 (for the most recent plan, see NEI, 1999). The other institutes produced plans in 1999 or 2000. In all cases, there was extensive participation of nonfederal scientists and nonscientists representing health groups.

A survey of recent strategic plans shows that they differ from institute to institute in their scope and level of detail. Some are just a few pages in length. Several are 75 pages or more. All the plans identify areas of promising research in which advances would help achieve each goal, but only some discuss possible programs or mechanisms, such as new center programs, as possible program initiatives.

For example, the strategic plan of National Institute of Allergy and Infectious Diseases (NIAID) has four major goals and also four "selected

[1] "In exercising the overall authority to oversee and coordinate the priority-setting process, the NIH director should receive from the directors of all of the institutes and centers multiyear strategic plans, including budget scenarios, in a standard format on an annual basis" (IOM, 1998:52).

crosscutting elements." One crosscutting element is "translation of research" from fundamental discoveries to new and improved treatments. The plan mentions a number of research mechanisms employed by NIAID to support translational and clinical research. "In extramural laboratories, for example, when transitional and applied research require shared resources, and/or a cross-disciplinary research team, program projects and center grants (P01, P30, P50) can facilitate the necessary linkages." NIAID also uses U01 and U19 cooperative agreements to support centers, which permit substantial involvement of NIAID program staff (examples include the STD [sexually transmitted disease] and Hepatitis C Cooperative Research Center Programs) (NIAID, 2000:89).

The National Cancer Institute (NCI) has the unique authority, termed the bypass budget, to submit a budget to the President without change by DHHS or OMB. The process for producing the bypass budget was changed in fiscal year (FY) 1998 to become more like a strategic planning exercise. Every three years, the plans identify and discuss in some detail a set of major research opportunities, including research goals, possible program initiatives, and suggested funding levels. Several new center programs were proposed in bypass budgets, including the In Vivo Cellular and Molecular Imaging Centers, Transdisciplinary Tobacco Use Research Centers, and Centers of Excellence in Cancer Communications Research, all supported by P50 center grants. "Building the nation's cancer research capacity" is a goal in the latest plan, in which the expansion of the P30 cancer centers, Specialized Programs of Research Excellence, and other P50 centers of excellence would play a major role (NCI, 2002).

The strategic plan of the National Heart, Lung, and Blood Institute (NHLBI) is organized around seven major program areas, each containing about five goals. For NHLBI, like NIAID, the center mechanism facilitates translational research, and one potential FY2003 initiative was to establish centers for translational research in peripheral and pulmonary vascular diseases. "A program of closely integrated, multidisciplinary research projects linking basic and clinical investigations is needed to lead to the development of improved therapeutic and preventive approaches for these diseases" (NHLBI, 2000).

The National Institute of Neurological Disorders and Stroke (NINDS) plan has a section on research infrastructure, which has new funding mechanisms as one goal. "For many of the exciting scientific opportunities described above, the current culture of individual investigators carrying out all phases of a project must be complemented by one in which collaboration among laboratories with different expertise is the norm" (NINDS, 1999). The plan listed a number of ways to facilitate research collaborations, such as core grants to groups of funded investigators at an institution, regional facilities for large-scale resources not fully justified at a single institution,

small grants to support the development of collaborations by funded investigators at different institutions, and grants to support the organization and functioning of consortia formed to address a specific problem.

Some institutes also develop strategic plans for specific problems. The National Institute of Child Health and Human Development (NICHD) has several focused plans for topics such as developmental biology, reproductive health, and SIDS (sudden infant death syndrome). NIAID has developed a strategic plan for biodefense research that lays out goals in six areas, for example, biology of the microbe, vaccines, and diagnostics. Another area is research resources, in which the plan says that the development of centralized sources of expertise in bioterrorism areas will be needed to speed the development of new products, tools, and interventions. The first goal in research resources is "Developing 6 to 12 Centers of Excellence for Bioterrorism and Emerging Diseases Research" (NIAID, 2002). A Request for Applications (RFA) for such centers was issued later in 2002, to be supported by U54 cooperative agreements, along with an RFA for Cooperative Centers for Translational Research on Human Immunology and Biodefense, to be supported by U19 cooperative agreements or R21 exploratory/developmental research project grants.

ANNUAL PROGRAM PLANNING AND BUDGETING PROCESS

The institutes begin to plan two years before the fiscal year begins, because NIH has to send a preliminary budget to the Secretary of Health and Human Services each June for the fiscal year beginning nearly 16 months later. For example, institute directors had to decide on changes they wanted in existing programs and new initiatives for FY2004 during the latter half of 2002 and early 2003 to be ready to work with the NIH director on their budget requests during April and May 2003. Each institute has its own process for program planning and decision making, culminating in a proposed budget request to the NIH director. In each case, the process is complex and includes input from a number of outside sources, including NIH advisory bodies, scientific workshops and conferences, and professional and consumer health groups (see next section). The institute directors, however, working with the NIH director, make the final decisions on what goes forward to the department and White House.

Institute-Level Planning and Budgeting

Each institute has its own system. Examples are described briefly here to impart a sense of what happens in a few concrete cases.

NIAID, in 1988, was one of the first to develop a formal planning process. "The structured process involves a progression of decision-making

events, informed by a continuous stream of reviews, evaluations, and consultations" (NIAID, 2000). The NIAID planning process is organized around two major events attended by the institute director, scientific program heads, and senior management staff (IOM, 1998:50). The Summer Policy Retreat is held to discuss and reach consensus on future scientific directions. At the second meeting, the Winter Policy Review, NIAID division directors make formal presentations on the state of knowledge, emerging public health needs, and research opportunities in their areas, and propose approaches for responding to the needs and opportunities that have been identified. At this time, specific initiatives are ranked in priority order within a budget target provided by the institute budget office. At their fall meeting, the NIAID national advisory council is provided an overview of the concepts and ideas discussed at the Summer Policy Retreat and asked for input, as are the council's subcommittees for the three extramural program divisions. After the Winter Policy Review, the divisions submit fully developed proposals for their high-priority initiatives, and the director of NIAID selects the initiatives that will be in the institute's budget submission. At the next meeting of the national advisory council, the divisions present the concepts for research initiatives for approval that are expected to be implemented through Program Announcements (PAs), RFAs, or Requests for Proposals (RFPs). Throughout the process, the NIAID director, division directors, and program staff interact with the institute's scientific and lay stakeholders; consider the results of scientific workshops, blue-ribbon panels, and program reviews; and respond to the priorities of the NIH director, the department, and Congress.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has a similar process organized around two documents presented to the institute's national advisory council each year. Together, they constitute the NIDDK Program Plan. Research Progress Reviews, which report on recent major scientific accomplishments, are presented to the council in February. Program Initiative Concepts are the second part of the Program Plan and are basically a list of potential new programs put forth by NIDDK's three extramural scientific operating divisions (NIDDK, 2000). Preliminary program initiatives are discussed with each division's subcommittee of the national advisory council. In September, after final selections by the institute director, Program Initiative Concepts are presented to the full national advisory council for review and approval.

NIH Director-Level Planning and Budgeting

The NIH director works with the institutes to prepare the NIH-wide budget request, which goes to the department for consideration in June. The director has final approval authority on the distribution of funds among

mechanisms and institutes. At all stages of the budget, the amount of funding for Research Project Grants, especially for new and competing renewal grants, is scrutinized closely, relative to the amounts for other mechanisms, such as centers and contracts.

In recent years, NIH directors have increasingly used their budget authority to stimulate trans-NIH programs. Harold Varmus, when he was director of NIH, identified crosscutting research opportunities, called Areas of Research Emphasis, and looked more favorably on requests for increases that addressed them. Since FY1991, NIH directors have had a director's discretionary fund and authority to transfer up to 1 percent of an institute's budget to adjust to changing priorities such as health emergencies. Dr. Varmus used these authorities to address NIH-wide priorities, for example, expansion of the mouse genetic sequencing center program.

The current NIH director, Elias Zerhouni, undertook a strategic planning exercise soon after he became director in May 2002. He convened intramural and extramural scientists from academia and industry to identify needed resources, roadblocks, and gaps in knowledge that no single NIH institute could provide in areas such as bioinformatics, molecular libraries, systems biology, and clinical research. The result was a "Roadmap Initiative" with three broad themes to guide NIH: (1) finding new pathways to discovery, (2) creating the research teams of the future, and (3) reengineering the clinical research enterprise. The Roadmap areas were published in the NIH budget request for FY2004 but will affect the FY2005 budget more, because the former was largely completed when the Roadmap came out.

Dr. Varmus also promoted the use of multi-institute and, in some cases, all-institute PAs and RFAs. Increasingly, trans-NIH and interagency coordinating committees are established to oversee the development of multi-institute initiatives, including the center programs for autism, muscular dystrophy, neuroinformatics, and Parkinson's disease research. More recently, trans-NIH working groups and task forces, including extramural researchers and representatives of VHAs as well as NIH staff, have been appointed to provide advice, for example, on implementation of the Parkinson's disease research agenda and development of initiatives in muscular dystrophy research.

Administration-Level Budget Process

In working with the institutes, the NIH director takes account of the program priorities and initiatives of the Secretary of Health and Human Services. The director then interacts with the department as it reviews NIH's preliminary budget estimate. In August the department gives NIH a budget "mark" for submission to OMB. The main submission is the NIH

mechanism table. After OMB gives NIH its budget mark in late November, the NIH director consults with the institute directors and departments to decide whether to appeal the initial OMB mark in budget hearings held by OMB, and later, to the President.

After the final budget amount for NIH is settled, NIH revises the budget to fit and 26 detailed Congressional Justification Budgets (CJs) are prepared and submitted to Congress (one each for the 24 grant-making institutes and centers, Office of the Director, and Buildings and Facilities).

Congressional Budget Process

In the spring, the NIH director and institute directors present the President's budget to the House and Senate Labor, Health and Human Services, and Education Appropriations Subcommittees. During the summer and fall, the appropriations subcommittees mark up the President's budget by institute and center. After the appropriations bills are passed, differences between the House and Senate are resolved in a conference committee. The NIH budget is adjusted again, at which point the final decisions on new program initiatives are made by the institute directors.

The appropriations process may have its own impact on new programs. The appropriations subcommittees for NIH do not put much detail in law, usually just the total appropriation amount for each institute. Instead, they use the reports that accompany bills to influence NIH, up to and including mandatory directives, for example, to establish a center program. When the budget becomes law, there are three reports—the House report, Senate report, and report of the conference committee negotiated between the House and Senate on the final appropriations bill—and any directives in the report of one committee remain in effect unless contradicted in the report of the other subcommittee or the conference committee report. Although report language does not have the force of law, NIH tries hard to comply, because they have to appear before the appropriations subcommittees every year for funding.

In recent years, the appropriations subcommittees have generally avoided being very directive in report language, although the degree of directiveness has varied by congressional branch, individual chairmen, and, occasionally, the chairman of the full appropriations committee.

There were more specifications, or "earmarking," of amounts of funding for a particular program, and of mechanisms such as centers, in earlier years, but earmarks created conflict in the early 1990s. NIH was experiencing flat budget growth, and earmarks had to be paid for with cuts in other programs. The 1988 IOM committee on priority setting at NIH analyzed report language accompanying the FY1993 and FY1998 budgets and found there were many more specific items in 1998, but they were much less

directive than in 1993 (IOM, 1998), and that approach has continued. The FY2002 report of the House subcommittee, for example, says:

> To enhance NIH's flexibility to allocate funding based on scientific opportunity, the Committee has attempted to minimize the amount of direction provided in the report accompanying the bill. For example, there are no directives to fund particular research mechanisms, such as centers or requests for applications, or specific amounts of funding for particular diseases (U.S. Congress, 2001a).

The Senate appropriations report for FY2002 said the subcommittee did not earmark specific funding levels for individual diseases and conditions, although there were some earmarks for funding certain programs. The Senate subcommittee said it strongly supported NIH "in the firm belief that sustained and sufficient funding is essential to accelerate the pace of research advances, ensure the timely application of new discoveries into clinical practice, and maintain the Nation's research infrastructure," but, it added, "an investment of this magnitude demands accountability" (U.S. Congress, 2001b).

The House and Senate reports for FY2002 appropriations refer to approximately 15 and 25 specific center programs, respectively. The House report generally urges an institute or the NIH director to "enhance" research in an area "through all available mechanisms, as appropriate, including establishing centers of excellence;" "commends" the institute for supporting existing centers; or "encourages" establishment or expansion of center programs. The Senate report also commends and encourages use of centers but also uses somewhat stronger language ("The Committee strongly supports the creation of new interdisciplinary centers to focus on…") or "encourages" or "strongly urges" funding of a specific number of new or additional centers. The report strongly urged establishment of at least three centers of excellence for muscular dystrophy research, although a specific number had been dropped from the authorization bill before it became the law.

Interpreting report language is done by those experienced in the legislative process, who must decide whether a particular phrasing means NIH must do something, should do it if possible, or can safely ignore an item in a report. NIH officials may contact the appropriations subcommittees to clarify intent. In the case of muscular dystrophy research, NIH (through an interinstitute task force) decided to set aside funding for two to three centers in the first RFA, issued in December 2002, and announced its intention to reissue another RFA in 2004 to reach a total of at least three centers. In addition, NIH decided to issue an RFA in early 2003 to award four to five planning grants to increase the number of places able to submit full center grant applications in 2004. NICHD has also issued an RFA to establish

three fragile X research centers, the number mandated in the Children's Health Act of 2000. In that case, however, after consultation with Congress, the institute decided to limit applicants to existing Mental Retardation Research Centers supported by NICHD. In the other cases where report language urged the establishment or expansion of center programs, NIH has decided not to do so, although it may take other initiatives, such as an RFA for individual-investigator or program project grants or to establish a clinical trials network.

In recent years, the House and Senate authorizing committees have become much more active in passing laws affecting NIH. Earlier, the committees passed an NIH reauthorization bill every three to four years, but they have not been able to pass one since the 1993 NIH Revitalization Act expired in 1996, because of conflicts over amendments to ban use of fetal tissue and similar issues. At that point, the authorization committees began to pass narrow bills addressing specific problems. These authorization bills have been the source of recent congressional mandates to create new center programs (e.g., for research on Parkinson's disease, autism, fragile X syndrome, muscular dystrophy, and rare diseases).

The appropriations subcommittees do not have to fund programs created or expanded by the authorizing committees, but typically they try to support newly authorized activities. For example, the Senate subcommittee strongly urged establishment of at least three centers for muscular dystrophy research and encouraged the institute "to provide sufficient funds for this purpose." The subcommittee called for the establishment of the three fragile X centers authorized by the Children's Health Act of 2000 and strongly urged NICHD "to allocate sufficient funds for that purpose." Regarding autism, the subcommittee said it wished to see "meaningful implementation of the new Centers of Excellence in Autism Research mandated in the Children's Health Act of 2000" and urged the NIH director "to allocate sufficient resources" to advance research on autism spectrum disorders (U.S. Congress, 2001b).

ADVISORY GROUP INPUT

NIH has an elaborate structure of outside advisory groups and other mechanisms for obtaining outside advice on health needs and scientific opportunities and ideas for new program initiatives. Some advisory groups are standing bodies with rotating memberships from the scientific community and the public, who play a regular role in the annual program planning and budgeting process and reviewing programs and new initiatives. NIH maintains more than 140 chartered advisory committees, more than any other federal agency.[2] Most of these committees are peer review groups

[2]http://www1.od.nih.gov/cmo/about/index.html.

engaged in evaluating applications for funding. Some are standing *program* advisory committees, and many are ad hoc groups, formed to provide advice on a specific topic, review a particular program, or develop a research agenda for a major area of science. Sometimes, advisory groups recommend establishment of research centers, or they may recommend initiatives the NIH staff decides would best be implemented through centers.

National Advisory Councils

Each institute and center has a national advisory council or, in the case of NCI, a national advisory board. In most cases, there are 18 members, 12 from the health and scientific disciplines and 6 representatives of the public. The Secretary of Health and Human Services appoints the members except in the case of the National Cancer Advisory Board (NCAB), which is appointed by the President.

The national advisory councils, although advisory, have an unusual role in government decision making. By law, they must review and approve all research grants and contracts awarded by NIH. They are also charged with providing advice on policies and programs, although the arrangements for this are left to the discretion of each institute director (NIH, 1995). Each institute involves its council in the annual program planning and budgeting process and strategic planning exercises in some way. In the examples described above, the national advisory councils participate at several points, providing feedback on priorities and needs early in the process and reviewing and approving new concepts for PAs, RFAs, and RFPs. At NCI, the chair of NCAB and chairman of NCAB's Planning and Budget Subcommittee serve on the Bypass Budget Planning Committee.

Program Advisory Committees

The NIH director has a number of advisory committees, including the Advisory Committee to the Director (ACD), Director's Council of Public Representatives, Office of AIDS Research Advisory Council, and Advisory Committee on Research on Women's Health (the last two advise the heads of program offices in the Office of the Director, the Office of AIDS Research, and Office of Research on Women's Health).

The ACD was created in 1966 in response to a review of NIH conducted by a blue-ribbon panel appointed by the White House Office of Science and Technology. According to its charter, the ACD advises the director on biomedical research, medical science, and biomedical communications and can make recommendations concerning program development, resource allocation, administrative regulation and policy, and other aspects

of NIH policy.[3] ACD working groups have studied and reported on gene transfer, clinical research, construction of research facilities, and biomedical computing. The last study resulted in a PA for planning National Programs of Excellence in Biomedical Computing, supported by 17 institutes, using a center mechanism (P20 developmental grants).

The Director's Council of Public Representatives was established in 1998 in response to a recommendation by an IOM committee (IOM, 1998). Its function is to consult with, advise, and make recommendations to the NIH director on issues and concerns important to the broad development of NIH programmatic and research priorities.[4]

Some of the institutes have standing program advisory committees. NCI has an advisory committee to the director, a Board of Scientific Advisers (to oversee extramural programs), and the NCI Director's Consumer Liaison Group. NHLBI has advisory committees for specific programs (sickle cell disease and sleep disorders). NIAID has similar advisory committees (for AIDS research and chronic fatigue syndrome). NICHD and the National Institute of Environmental Health Studies have advisory bodies for medical rehabilitation research and alternative toxicological methods, respectively.

All the institutes appoint ad hoc bodies (committees, working groups, task forces, or panels) to evaluate programs, assess the state of the science, and develop research agendas. The reports of these groups are another input into the planning process. Some groups consider mechanisms and may recommend the establishment of centers. For example, when medical imaging was identified as a priority in NCI's planning process, the NCI director appointed an Imaging Sciences Working Group. The Working Group report contained a number of recommendations, one of which was to create interdisciplinary "imaging centers of excellence."[5] The recommendation resulted in the establishment of In Vivo Cellular and Molecular Imaging Centers in 2000.

NCI has also convened a series of Progress Review Groups to assess the state of science concerning a particular type of cancer, develop a research agenda, and recommend high-priority programs needed to make progress in addressing the disease. Some have recommended center programs. The Pancreatic Cancer Progress Review Group, for example, identified three key strategies to speed research and treatments, one of them the establishment of centers of excellence for pancreatic cancer research and care. "Centers of excellence in pancreatic cancer would optimize both research and

[3]http://www.nih.gov/about/director/acd.htm.
[4]http://copr.nih.gov/mission_charter.shtm.
[5]www3.cancer.gov/dip/ISWG3.htm.

patient outcomes and facilitate the diffusion of knowledge into the community. These centers would offer broad clinical expertise, thereby attracting significant patient volume; provide state-of-the-art diagnosis and treatment; and bring together scientific investigators evaluating issues critical to this disease" (NCI, 2002).

In 1997 the NIH Office of Rare Diseases convened a Special Emphasis Panel to develop recommendations for stimulating and coordinating research on rare diseases. The panel's January 2001 report recommended that NIH support the establishment of Specialized Research and Diagnostic Centers of Excellence for Rare Diseases to stimulate research, provide research training, and aid in the diagnosis of rare diseases. The panel also suggested using established centers, such as General Clinical Research Centers, as the infrastructure for creating research and diagnostic services related to rare diseases.[6] As a result, NIH issued an RFA in early 2003 to establish a network of clinical centers for research on rare diseases.[7]

Sponsorship of Scientific Workshops

The institutes convene workshops on a regular basis to help them plan activities in a particular area of science or to address a specific disease or condition. Many workshop reports are posted on institute websites and are referred to in program descriptions and in PAs, RFAs, and RFPs. Workshop reports were involved in the genesis of several recent center programs, for example, Centers of Excellence in Chemical and Library Development, Centers for Human Embryonic Stem Cell Research, and Centers of Excellence in Complex Biomedical Systems Research, and Autism Centers of Excellence.[8]

Ongoing Interactions with Constituency Groups

Each institute's director and extramural program heads meet regularly with representatives of VHAs, patient advocacy groups, and scientific and medical associations. The NIH director and NCI director have formal consumer advisory groups that meet several times a year. Program staff at all levels participate in annual meetings of scientific and medical associations and some hold focus sessions at these meetings on topics of interest.

---

[6]rarediseases.info.nih.gov/news-reports/fy99annual/SEP.html.

[7]RFA-RR-03-008.

[8]The workshop reports are at: www.nigms.nih.gov/news/reports/chemical_diversity.html, www.nigms.nih.gov/news/reports/stemcellwork shop.html, www.nigms.nih.gov/news/reports/complexbio.html, and www.nichd.nih.gov/publications/pubs/autism/index.htm, respectively.

In addition, some program advisory groups have members representing voluntary health agencies and disease advocacy groups. The institutes each have an Office of Public Liaison, and the NCI director has a Consumer Liaison Group. The NIH director has several advisory committees, the Advisory Committee to the Director, and the Director's Council of Public Representatives.

The institutes have extensive ongoing arrangements for obtaining external views and advice from both the research community and the public, and consult with their national advisory councils on program priorities and balance among mechanisms. In some areas of research, external committees have created research plans that identify research needs and consider mechanisms for addressing them, including centers. Increasingly, the strategic plans the institutes develop with external professional and public participation are addressing implementation strategies, including the appropriate mix of mechanisms.

PROGRAM IMPLEMENTATION PROCEDURES

NIH implements new center programs by publishing invitations to apply for funding in the *NIH Guide for Grants and Contracts*, which is published daily. The invitation can be in several forms. It may be a PA, which notifies the research community that NIH is interested in funding quality applications for centers in specific areas. Most new center programs are launched with an RFA, which differs from a PA in several important ways. It has a one-time deadline, and it must state how much money has been set aside and approximately how many centers NIH expects to fund. In a few cases, centers are funded by contract, and RFPs are issued. If a PA is used to initiate a new center program, it is either a PAR, in which the applications are reviewed by the institute rather than the Center for Scientific Review, or a PAS, in which the applications are reviewed by the institute and the funding is formally set aside, as with an RFA.

Institutes wishing to use a PA or RFA must follow certain common procedures laid out in the *NIH Manual*. The institute must submit a package with the draft PA or RFA to the Office of Extramural Programs in the Office of the NIH Director for review to see that certain steps were taken and that the document is in the proper format and contains the required provisions. (The NIH contracts office oversees a similar process for clearing RFPs.)

The key procedural requirements are:

- The institute must document the clearance of PA and RFA concepts (i.e., purpose, scope, and objectives) for "relevance, priority, and need. This clearance must include advice from the public and may be obtained through,

for example, consultation with national advisory councils and advisory boards, Congressional mandate, or workshops convened specifically for advisory purposes" (NIH, 1994).

- If the concept is approved and funded, the institute's grants management officer must review and comment on the proposed PA or RFA, including certification that the proper mechanism of support was chosen, and the institute's chief scientific review official, who will be responsible for the review of the applications, is also supposed to review the proposed PA or RFA.
- At least a month before the planned publication date, the institute uses an electronic early notification system to alert other institutes and let them express any concerns about significant overlap with their programs. If so, an accommodation is worked out. An affected institute may, for example, cosponsor and jointly publish a PA, agree to fund certain RFA applications after they have been reviewed by the peer review group in the lead institute, or agree to cofund each award (which involves a transfer of funding to the lead institute).
- The extramural program policy officer in the Office of Extramural Programs checks to see that proper procedures have been followed and that the PA or RFA is consistent with NIH and Public Health Service policies (i.e., if it is an RFA, the estimated set-aside for funding and approximate number of centers are specified).
- Cooperative agreements, because they entail substantial participation by NIH staff, undergo additional central scrutiny. The institute is required to submit a justification memorandum, along with a draft of the RFA, to the associate director for extramural affairs of NIH. The memorandum must justify the rationale and need for the cooperative agreement rather than the contract mechanism and for the substantial scientific and programmatic involvement by NIH staff. The cooperative agreement RFA has to have language that outlines the responsibilities and rights of the grantee, nature and extent of institute staff involvement, and collaborative responsibilities, as well as a mechanism for arbitrating disagreements between grantees and the institute (NIH, 1993).

Each institute has its own policies and procedures for deciding whether or how to establish a new program or initiative and develop the PA, RFA, or RFP, including review and approval of the concept paper. In most cases, this is done by the national advisory council as an integral part of the annual program planning and budgeting process within an institute. In this way, approval of a new center program is fulfilled by review and approval of the concept paper for a PA, RFA, or RFP. As shown above, for example, the second part of NIDDK's annual Program Plan is called Program Initiative Concepts, which is the final set of initiatives approved by the institute

director and submitted to the NIDDK national advisory council each September.

At NIAID, an "initiative" *is* a PA, RFA, or RFP.[9] A "concept" is the earliest planning stage of an initiative.

> Concepts for future initiatives are the fruits of many meetings and focus groups with the extramural community. These information exchanges blend ideas of the community with those of NIAID staff into a solid understanding of future scientific needs and directions. These ideas are then discussed at NIAID's biannual planning meetings where Institute managers view the big picture and decide which concepts to send to Council for review.[10]

At NIAID, "concept clearance" is a mandatory review of each initiative, generally performed by the subcommittees of NIAID's national advisory council that oversee each of the institute's extramural divisions. "For each concept, the subcommittee looks deeply at its scientific merit, relative priority, appropriate budget, and funding mechanism.[11] "After hearing staff presentations, Council recommends approval of an initiative, its budget, and mechanism (e.g., grant or contract, and grant type) and advises on scientific matters.[12] Not all concepts approved by the council are implemented (i.e., published as initiatives). Implementation depends on the institute-wide scientific and programmatic priority of the initiative and the amount of funds available.

The national advisory council of the National Center for Complementary and Alternative Medicine approved the concepts for Complementary and Alternative Medicine Research Centers and Developmental Complementary and Alternative Medicine Research Centers in August 2002. The reasons for establishing centers appear in several places. The background discussion section says: "Research centers provide a special opportunity to bring together the resources necessary for the rigorous scientific investigation of CAM [Complementary and Alternative Medicine]." The section on purpose reads: "The purpose of this initiative is to promote innovative, high quality, multidisciplinary basic research through clinical research in the area of complementary and alternative medicine. This will be accomplished by providing support for research centers to conduct integrated studies…." There is a justification of the proposed funding mechanism, in this case the program project (P01) grant:

---

[9]See NIAID's glossary of funding and policy terms at www.niaid.nih.gov/ncn/glossary, 5-2-03.

[10]www.niaid.nih.gov/ncn/budget/concpt.htm, 5-2-03.

[11]www.niaid.nih.gov/ncn/budget/concpt.htm, 5-2-03.

[12]www.niaid.nih.gov/ncn/glossary, 5-2-03.

> This type of award supports broadly based multidisciplinary research programs that have a well-defined central research focus or objective. An important feature is that the interrelationships among the individual scientifically meritorious projects will result in a greater contribution to the overall program goals than if each project was pursued individually.... The award also can provide support for certain common resources termed cores.[13]

Concept clearance does not have to be performed by a national advisory council. As already seen, concept clearance at NIAID is performed by subcommittees for each program division during regular council meetings and ratified by the full council. NIDDK has a similar system. According to the *NIH Manual*, concepts for initiatives can be reviewed and approved by any chartered advisory body, including program advisory committees and special emphasis panels (NIH, 1994).

At NCI, concepts are reviewed by the Board of Scientific Advisers (BSA), which was established to advise on extramural programs. It is linked to the institute planning process by membership of the BSA chairman on the Bypass Budget Planning Committee. The NCI executive committee and then the BSA see a document that contains the narrative material for the proposed PA or RFA and additional information. The narrative justification for Centers of Excellence in Cancer Communications Research, for example, was 10 pages in length, with an overview, background, RFA purpose, and research questions (including a detailed list of potential research topics). The text of these sections of the concept paper appeared in the RFA.[14] In addition, there was an analysis of NCI's portfolio of cancer communications grants, justification of the award mechanism, budget information, and timeline (the last two also appear in the RFA). There was a list of 24 scientific references. According to the mechanism justification:

> The NCI's P50 centers mechanism was chosen because of its stated objective of translating basic research findings into applied, innovative research with patients and populations, with the ultimate objective of reducing cancer risk, incidence and mortality, and improving quality of life. Centers include fully developed research projects, innovative pilot projects, a career development program, cores, and other resources dedicated to translational research objectives... By emphasizing meaningful integration and collaboration among scientists, the Centers will provide a challenging and unique venue for training the next generation of health communication researchers.[15]

---

[13] nccam.nih.gov/research/concepts/consider/centers.htm, 5-2-03.
[14] grants.nih.gov/grants/guide/rfa-files/RFA-CA-01-019.html, 5-2-03.
[15] dccps.nci.nih.gov/communicationcenters/about_just.html.

Not all concepts submitted by the institutes are approved. For example, there was a debate about the proposed Centers of Excellence in Chemical Methodology and Library Development at the September 2000 meeting of the National Institute of General Medical Sciences (NIGMS) council. The proposal was sent back to "be reformulated to focus on the basic research component, to clarify the role of biologists in a program targeted to developing chemical methodologies, and to reassess the mechanism by which this program should be supported.[16] After the concept was modified by adding a requirement for a library synthesis core to clarify the intended focus on combinatorial chemistry methods development and be a clear point of contact for the biology research community, it was passed at the next NIGMS council meeting in January 2001 (the RFA was published in June 2001).

If an RFA or PA is reissued, some but not all institutes require another concept approval by the national advisory council or other advisory body, while others rely on the initial approval, although the RFA or PA is often revised. Also, from time to time, a center program is changed substantially or discontinued entirely, although in the latter case, it is usually replaced by a new center program. Recent examples include changes in the NHLBI Specialized Centers of Research program, symbolized by a name change to Specialized Centers of Clinically Oriented Research; discontinuation of the National Institute of Arthritis and Musculoskeletal and Skin Diseases Multipurpose Arthritis and Musculoskeletal Diseases Centers, replaced by Multidisciplinary Clinical Research Centers for Arthritis and Musculoskeletal and Skin Diseases; and a change from supporting Population Research Centers with a P30 center core grant or a P50 specialized center grant to supporting their research infrastructure with the R24 resource-related research project grant. These and similar cases of changes in or discontinuations of center programs often result from outside reviews, which are addressed more fully in Chapter 5 on evaluation.

REFERENCES

IOM (Institute of Medicine). 1998. *Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health*. Washington, DC: National Academy Press.

NCI (National Cancer Institute). 2002. *Strategic Plan for Addressing the Recommendations of the Pancreatic Cancer Progress Review Group*. [Online]. Available: http://prg.cancer.gov/pancreatic/pancreatic.pdf [accessed December 15, 2003].

[16]www.nigms.nih.gov/ about_nigms/council_sept00.html, 5-2-03.

NEI (National Eye Institute). 1999. *Vision Research - A National Plan: 1999-2003*. [Online]. Available: http://www.nei.nih.gov/resources/strategicplans/plan.htm [accessed December 15, 2003].

NHLBI. (National Heart, Lung, and Blood Institute). 2000. *NHLBI Strategic Plan FY 2003-2007*. [Online]. Available: http://www.nhlbi.nih.gov/resources/docs/plan/index.htm [accessed December 15, 2003].

NIAID (National Institute of Allergy and Infectious Diseases). 2000. *Planning for the 21st Century*. [Online]. Available: http://www.niaid.nih.gov/strategicplan2000/pdf/strategicplan.pdf [accessed December 15, 2003].

NIAID. 2002. *NIAID Strategic Plan for Biodefense Research*. [Online]. Available: http://www.niaid.nih.gov/biodefense/research/strategic.pdf [accessed December 15, 2003].

NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases). 2000. *NIDDK Strategic Plan.* [Online] Available: http://www.niddk.nih.gov/federal/planning/stratplan-2000.htm.

NIH (National Institutes of Health). 1993. Implementation of cooperative agreements. In: *NIH Policy Manual,* Chapter 4815. Bethesda, MD: NIH (Available from the Office of Extramural Programs, Office of the Director, NIH).

NIH. 1994. Program announcements and requests for applications. In: *NIH Policy Manual,* Chapter 4110. Bethesda, MD: NIH (Available from the Office of Extramural Programs, Office of the Director, NIH).

NIH. 1995. Management and procedures of national advisory councils and boards in their review of extramural activities. In: *NIH Policy Manual,* Chapter 4513. Bethesda, MD: NIH (Available from the Office of Extramural Programs, Office of the Director, NIH).

NIH. 2001. *Setting Research Priorities at the National Institutes of Health*. Revised edition. [Online]. Available: http://www.nih.gov/about/researchpriorities.htm [accessed December 15, 2003].

NINDS (National Institute of Neurological Disorders and Stroke). 1999. *Neuroscience at the New Millennium: Priorities and Plans for the National Institute of Neurological Disorders and Stroke, Fiscal Years 2000-2001*. [Online]. Available: http://www.ninds.nih.gov/about_ninds/strategic_plan.htm [accessed December 15, 2003].

U.S. Congress. 2001a. H.R. 3061, Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriation Bill, 2002. House Report 107-229. Washington, DC.

U.S. Congress. 2001b. S. 1536, Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriation Bill, 2002. Senate Report 107-84. Washington, DC.

E

Justifications for Center Programs Used in Recent RFAs and PAs

1. The scientific opportunities and/or public health needs that the center program addresses have high priority.

Excellence in Partnerships for Community Outreach, Research on Disparities in Health and Training (Project EXPORT). Consistent with the goals of the trans-NIH Strategic Plan, EXPORT Centers will focus on research aimed at reducing and eliminating health disparities, improving research capacity, and providing outreach and education (RFA-MD-03-002).

Centers of Excellence in Chemical Methodologies and Library Development. Consistent with the stated mission of the National Institute of General Medical Sciences (NIGMS), which is to support "basic biomedical research that is not targeted to specific diseases, but that increases understanding of life processes...," the rationale behind this RFA is that advances in fundamental, enabling methodologies for diversity-oriented synthesis will produce lasting benefits for all of biomedical science, including biology and medicine (RFA-GM-01-006).

Centers for Oceans and Human Health. This RFA draws on the recommendations contained in the strategic plans of the Participating Agencies (NIEHS, 2000; NSF, 2000a, 2000b), those highlighted by the Ocean Studies Board of the National Research Council (NRC, 1999),

and those discussed at a government-sponsored Roundtable on Oceans and Human Health held in Research Triangle Park, NC, December, 2001 (RFA-ES-03-003).

Breast Cancer and the Environment Research Centers. Five scientific priority areas have been developed after a series of workshops and meetings held on this topic attended by scientists, representatives from breast cancer advocacy groups, and health care practitioners (RFA-ES-03-001).

Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. As identified by the recently convened National Institute of Allergy and Infectious Diseases (NIAID) Blue Ribbon Panel on Bioterrorism and Its Implications for Biomedical Research, there is a critical need for the establishment of highly developed research and development infrastructure with strong translational research capacity to implement the Biodefense Research Agenda of NIAID (RFA-AI-02-031).

Centers for Population Health and Health Disparities. This RFA draws on the recommendations contained in the strategic plans of the sponsoring National Institutes of Health (NIH) institutes concerning health disparities, those submitted to NIH from the conference entitled "Toward Higher Levels of Analysis: Progress and Promise in Research on Social and Cultural Dimensions of Health," and those highlighted by numerous recent National Academy of Sciences and Institute of Medicine Reports (RFA-ES-02-009).

Centers of Excellence in Cancer Communications Research. This initiative is the centerpiece of the National Cancer Institute's (NCI) Extraordinary Opportunity in Cancer Communications. The novelty and scope of this initiative reflects the NCI's recognition that effective communications can and should be used to narrow the enormous gap between discovery and applications and to reduce health disparities among our citizens....Potential applicants are encouraged to consult the NCI's Bypass Budget for background about the NCI's goals and progress in cancer communications (RFA-CA-01-019).

2. Centers would provide an organizational environment that facilitates activities that individual-investigator grants or other mechanisms of research support cannot easily provide.

These activities include:

- **Multidisciplinary collaborations for problems that require diverse scientific backgrounds.**

Centers of Excellence in Complex Biomedical Systems Research. NIGMS currently is committed to supporting the analysis of complex biological systems through investigator-initiated research project grants, using the R01, P01, R21, and other appropriate grant mechanisms. However, the resources needed to conduct the multifaceted, multidisciplinary projects that may be required to achieve significant advances in these complex areas may be beyond the scope of the typical R01 or P01 grant (RFA-GM-01-001).

Transdisciplinary Prevention Research Centers. It is expected that a transdisciplinary approach will bring diverse and multiple scientific perspectives to catalyze new thinking about prevention research questions. The scientific interactions and collaborations supported by this center model are intended to maximize scientific creativity and stimulate new developments in the field of drug abuse prevention research more rapidly than would be possible by depending on individual investigators working in relative isolation (RFA-DA-02-005).

Centers of Excellence in Chemical Methodologies and Library Development. The Chemical Methodologies and Library Development Centers will feature collaborations and team approaches that otherwise would not be established, including individuals from various subdisciplines within the field of chemistry and/or from cognate fields that will contribute toward the development of novel enabling methodologies (RFA-GM-01-006).

Centers for Oceans and Human Health (COHH). COHH are expected to create an environment conducive to interdisciplinary and reciprocally beneficial collaborations among biomedical scientists (e.g., epidemiologists, pharmacologists, toxicologists, microbiologists, cell and molecular biologists) and ocean scientists (e.g., biological and physical oceanographers, geochemists, and ecologists) with the common goal of improving our knowledge of the impacts of the ocean on human health (RFA-ES-03-003).

Exploratory Center Grants for Human Embryonic Stem Cell Research. … NIGMS hosted a workshop on the Basic Biology of Mammalian Stem Cells…The workshop report summarizes many fascinat-

ing opportunities to use HESC [human embryonic stem cells] to study important biological problems and identifies activities that need to be addressed in order to stimulate and facilitate the use of HESC as a model system. These activities include: continued interdisciplinary collaborations and discussions between stem cell researchers and basic biologists … (RFA-HL-03-003).

Network for Translational Research: Optical Imaging. It is anticipated that translational research will require broad, multidisciplinary teams. They should include representatives of fields necessary for successful completion of the proposed basic research and translational projects, and might include molecular biologists, chemists, physicists, optical and computer engineers, imaging scientists and physicians, among others (RFA-CA-03-002).

Regional Centers of Excellence (RCE) for Biodefense and Emerging Infectious Diseases Research. The intent of the RCE Program is to support any substantial range of research, training, and development activities as long as the plan involves vibrant, multidisciplinary approaches that transcend customary thinking and organizational structures to address critical questions related to the Centers for Disease Control and Prevention (CDC) Category A-C Agents from very basic to clinical (RFA-AI-02-031).

Centers for Population Health and Health Disparities (CPHHD). CPHHD are expected to create an environment conducive to interdisciplinary and reciprocally beneficial collaborations among biomedical scientists, social scientists, and affected communities with the common goal of improving population health and reducing health disparities (RFA-ES-02-009).

Centers of Excellence in Cancer Communications Research (CECCR). It is expected that the Centers' interdisciplinary efforts will result in new and/or improved syntheses, theories, methods, and interventions, including those for diverse populations.…It is expected that the CECCRs will catalyze problem solving and lead to more rapid advances in knowledge than would be possible by depending on individual investigators working in relative isolation (RFA-CA-01-019).

Institutional Center Core Grants to Support Neuroscience Research. Center Core Grants will foster a cooperative and interactive research environment through which multidisciplinary approaches to neuroscience problems and joint research efforts will be stimulated (PAR-02-059).

Fragile X Research Centers. The supplement within a P30 Center is designed to encourage and support broadly based multidisciplinary research programs that have a well-defined central research focus or objective in fragile X syndrome research. This supplement, the Fragile X Research Center, is based on a unique and new concept for the purposes of this RFA: a "Center within a Center." … An important feature of this new "Center within a Center" concept is that the interrelationships among the individual projects and Cores proposed for the Fragile X Research Center will result in a greater contribution to the overall MRDDRC [Mental Retardation and Developmental Disabilities Research Centers] goals than if each project was pursued independently (RFA-HD-02-009).

- **Multi-investigator teams capable of a scope of activities not possible with other funding mechanisms.**

Centers of Excellence in Complex Biomedical Systems Research. The Center Grant mechanism (P50), together with the Planning Grant mechanism (P20), will support the development of multi-investigator teams capable of engaging biomedical complexity with a scope of activities not possible with other funding mechanisms (RFA-GM-01-001).

Centers of Excellence in Chemical Methodologies and Library Development (CMLD). It is clear that innovations in one aspect of library methodology research will permit or even require complementary advances in others.…Thus, for maximum impact, Centers should feature broadly diversified research teams. While chemists from any subdiscipline may participate in a CMLD Center, collaborations that cross traditional subdisciplinary boundaries (e.g., organic, inorganic, analytical, physical, computational, and polymer chemistry) and that feature complementary (i.e., nonredundant) skills are particularly encouraged (RFA-GM-01-006).

Research Core Centers for Advanced Neuroinformatics Research. The aim is to assemble teams of peer reviewed, federally funded, basic and clinical neuroscience investigators from diverse institutions by providing additional excellent shared computer sciences research resources and facilities (e.g., for hardware and software development, and/or computer facilities, data processing and analysis) for their coordinated, collaborative activities (PAR-03-037).

Centers for Population Health and Health Disparities. Projects will bring together the skills of basic, clinical, and public health intervention

research scientists with other population research scientists, such as anthropologists, demographers, economists, epidemiologists, psychologists, sociologists, historians, and political scientists to support multiple levels of analysis within and/or across research projects supported by Center funding (RFA-ES-02-009).

Autism Research Centers of Excellence: The STAART Program. What distinguishes a research program that is appropriate for STAART [Studies to Advance Autism Research and Treatment] support from a research program that is better supported through a series of R01 grants? …Meaningful and committed interactions among the disciplines must be evident.…Results of one subproject may well affect the understanding and interpretation of data from another project and thereby influence the nature of the research being performed in one or more of the other subprojects. The feasibility of the research proposed on any subproject might be significantly diminished if that subproject were submitted as a traditional individual research grant (R01) application…the STAART Centers Program will represent a substantial increase in the scope of the scientific enterprise related to this disorder, particularly as it provides a specific emphasis on and direct funding for treatment research (RFA-MH-02-001).

- **Translation of basic research to clinical practice.**

Transdisciplinary Prevention Research Centers (TPRC). Transdisciplinary collaborations in these TPRCs should: (1) stimulate the translation of basic science discoveries (from both preclinical and human laboratory-based or field investigation) into the design of novel preventive interventions, and (2) capitalize on opportunities from drug abuse prevention research to inform the design of basic science investigations on vulnerability to drug abuse and addiction (RFA-DA-02-005).

Breast Cancer and the Environment Research Centers. The National Institute of Environmental Health Sciences and NCI invite applications to create a network of research centers in which multidisciplinary teams of scientists, clinicians, and breast cancer advocates work collaboratively on a unique set of scientific questions that focus on how chemical, physical, biological, and social factors in the environment work together with genetic factors to cause breast cancer. Answering these questions will allow the translation of such findings into information that can be applied to increase awareness of the causes of breast cancer (RFA-ES-03-001).

Muscular Dystrophy Cooperative Research Centers. In May 2002, NIAMS, NINDS, and NICHD brought together a Muscular Dystrophy Research Task Force to identify ways to increase the level of understanding of muscular dystrophies and improve diagnosis and treatment approaches.…Among other suggestions, the Task Force recommended support for research centers to promote the exchange of ideas and information between basic and clinical investigators. Such centers should have a broad approach…and plans to move new knowledge to a clinical setting.…The close interaction between basic researchers and clinicians will accelerate the translation of fundamental advances to the clinic and the utilization of patient materials for basic research (RFA-AR-03-002).

Cooperative Centers for Translational Research on Human Immunology and Biodefense. This program is expected to substantially support the biodefense effort by providing stable funding for immunology Centers focused on the translation from animal to human research (RFA-AI-02-042).

Centers of Excellence in Cancer Communications Research. Bringing people together from different disciplines can accelerate the speed with which discoveries are made, translated into researchable hypotheses and then developed into products that benefit people…there should be a focus on translatability—from basic to intervention research to dissemination and sometimes back again (RFA-CA-01-019).

- **Complement existing and stimulate new investigator-initiated applications for research project grants.**

Network for Translational Research: Optical Imaging. Developments that successfully translate to clinically feasible or research-oriented instruments and methods are expected to stimulate investigator-initiated applications for clinical and basic research grants under other support mechanisms, such as the R01, R21, R21/R33, R33, R41, R42, R43, and R44 (RFA-CA-03-002).

Muscular Dystrophy Cooperative Research Centers (MDCRCs). It is desirable for MDCRC-supported research to complement other funded research related to muscular dystrophy taking place at the applicant institution, including activities supported by R01, P01, and other mechanisms. It is anticipated that resources and projects that are in place with funding from sources other than the MDCRC Program will

synergistically interact with MDCRC infrastructure, cores, and projects. The application should explain how MDCRC support would facilitate the development and progress of related projects that may not be an integral component of the MDCRC itself (RFA-AR-03-002).

- **Cross-disciplinary or translational research training of graduate students, postdoctoral fellows, and other health professionals.**

Centers of Excellence in Complex Biomedical Systems Research. One reason for the current lack of adequately qualified personnel is that there are too few appropriate environments available to support this kind of training. The establishment of Centers under this program is intended to help alleviate this shortage by serving as an academic focus for systems approaches. To maximize their impact, Centers should integrate the training of young investigators and broaden the training of established investigators. Graduate students and postdoctoral fellows should participate in the research (RFA-GM-01-001).

Transdisciplinary Prevention Research Centers (TPRCs). Because it is intended that the these prevention research centers will provide ideal settings for training future generations of drug abuse prevention researchers in transdisciplinary sciences and translational perspectives, TPRC applications must have strong career development objectives (RFA-DA-02-005).

Muscular Dystrophy Cooperative Research Centers. Further, the [center] environment should promote cross-disciplinary research training (RFA-AR-03-002).

Cooperative Reproductive Science Research Centers at Minority Institutions. It is envisioned that each center will ultimately become a training and mentoring resource for developing and strengthening the research capacity of the nation by expanding opportunities for minority scientists, particularly those underrepresented within the scientific workforce (RFA-HD-00-019).

- **Attraction of experienced researchers into a new area of research.**

Centers of Excellence in Complex Biomedical Systems Research. In addition to research contributions, successful Centers will provide their home institutions with the means to implement organizational and professional changes that will make interdisciplinary research in com-

plex biological systems and bioinformatics attractive career options for both established and entry-level investigators (RFA-GM-01-001).

Comprehensive Centers on Health Disparities at RCMI-Eligible Institutions. Support will be provided to recruit established clinical researchers with an active research laboratory and independent research support. They will serve as mentors to junior researchers in basic or clinical research. These new faculty will receive support to establish their research laboratories, acquire specialized equipment, and hire postdoctoral fellows and technical assistants. It is anticipated that they will serve as magnet investigators for the recruitment of other research faculty who will complement the thematic focus of the application (RFA-RR-03-004).

Centers of Excellence in Chemical Methodologies and Library Development (CMLD). … it is evident that reliance on current techniques for producing and evaluating chemical libraries will limit the ability to capitalize on the plethora of new targets that will become evident through research in proteomics and functional genomics. The goal of the CMLD initiative is to address these limitations by attracting the best academic chemists to the development of a wide range of versatile, dependable library-related methodologies (RFA-GM-01-006).

Network for Translational Research: Optical Imaging. Involvement of basic and clinical scientists who may not have a specific research record in cancer research, but who have the potential to provide experience crucial for the success of this network are considered important (RFA-CA-03-002).

Autism Research Centers of Excellence: The STAART Program. It is also anticipated that STAART Centers will attract outstanding investigators who have not have been part of the autism field (RFA-MH-02-001).

- **Existence of a network of coordinated research activities with greater capacity than any single center, for example, in recruiting larger numbers of patients into common research protocols, pooling patient data and biological specimens on the scale necessary to identify biomarkers for disease risk, disease activity and severity, and clinical outcome, and improving methods and technologies.**

Rare Disease Clinical Research Network. The purpose of this cooperative research network is to facilitate clinical research in rare diseases

through support for (1) collaborative clinical research in rare diseases, including longitudinal studies of individuals with rare diseases, clinical studies, phase one and two trials, and/or pilot and demonstration projects.... (RFA-RR-03-008)

Network for Translational Research: Optical Imaging. The goal of this Request for Applications is to organize a consortium with flexibility in scope, funding, and incentives to encourage inter- and intrateam collaborations on translational cancer research ... by developing a consensus process to improve methods for system integration, optimization and validation of next-generation in vivo optical imaging and/or spectroscopy methods and technologies, including contrast agents (RFA-CA-03-002).

Cooperative Centers for Translational Research on Human Immunology and Biodefense. Synergistic interaction is a key feature of this program. Each Center will provide unique and complementary strengths in terms of technical potential and specific areas of immunological investigation, and all Centers will share responsibility for program development and resource coordination via a Centers Steering Committee (RFA-AI-02-042).

Autoimmunity Centers of Excellence. Because all these diseases will be increasingly approached with immunologic interventions, a cooperative group with the capability to evaluate a new agent in any of a number of diseases offers considerable advantages. Increased interaction of clinical specialists in planning, performance, and evaluation of trials/studies should lead to a more coordinated approach to development of new immune-based therapies for all autoimmune diseases (RFA-AI-98-010).

Autism Research Centers of Excellence: The STAART Program. In addition to these issues that are focused on individual centers, a major goal of the STAART Centers Program is to establish a major research network that, as a whole, will be capable of implementing large treatment, diagnostic, genetic, neuroscientific and other studies, which are not currently feasible (RFA-MH-02-001).

3. The center program would provide critical research resources needed for productive research that are difficult or too expensive to develop in most individual laboratories.

Neuroproteomics Research Centers. Current technology requires a sig-

nificant financial and educational investment to obtain, manage and interpret high-quality data. Thus, it is not feasible or practical for individual investigators to establish such a resource for use by their laboratory alone (RFA-DA-04-004).

Research Core Centers for Advanced Neuroinformatics Research. This Research Core Center PA is an institutional award…to support centralized resources and facilities shared by two or more investigators with existing funded research projects. Its goal is to encourage integrative, collaborative, interdisciplinary research approaches to more effectively and efficiently solve significant questions in basic and clinical neuroscience, that cross institutional and disciplinary boundaries (PAR-03-037).

Exploratory Center Grants for Human Embryonic Stem Cell Research. Exploratory Center Grants will be expected to: 1) establish and support institutional core facilities that can be used for the growth and maintenance of HESC, for the further characterization of HESC properties, and for development of reagents and tools that will enhance the use of HESC as a model system…. (RFA-HL-03-003)

4. *Development of research infrastructure.*

- **Institutional development of a field of research (nursing, population research)**
- **State-of-the-art biomedical and behavioral research at minority-serving institutions or institutions in regions with little NIH research funding**
- **Community education and outreach**

Excellence in Partnerships for Community Outreach, Research on Disparities in Health, and Training (Project EXPORT). These center grants will provide a mechanism to strengthen the infrastructure for minority health and other health disparities research and training as well as provide resources for the development of innovative partnership models (RFA-MD-03-002).

Comprehensive Centers on Health Disparities at RCMI-Eligible Institutions. In the long range, it is anticipated that this program will facilitate the development of the institution's clinical research capacity…. This RFA is one way that the NIH identifies and supports biomedical and clinical researchers at eligible institutions to conduct and report the meritorious research that will foster successful competition

for traditional research project grants (e.g., R-series and P-series) (RFA-RR-03-004).

Centers of Excellence for Research on Complementary and Alternative Medicine (CAM). Currently the Centers Program consists of three individual activities, each designed to meet a different need.…The Developmental Centers for Research on Complementary and Alternative Medicine are intended to promote development of CAM research expertise and infrastructure, support enhanced communication and partnership-building between CAM and conventional institutions/investigators and to support developmental research projects. The International Centers for Research on CAM are designed to establish partnerships and cross-cultural exchange through which foreign and U.S. institutions and investigators can collaborate to design and implement research on CAM/traditional indigenous medical systems or components thereof in the cultures and/or environments in which they originated. The Centers of Excellence for Research on CAM, described in this announcement, are designed to provide a vehicle for highly skilled and accomplished researchers to apply their expertise in addressing CAM research questions, with an emphasis on elucidating the mechanisms of action of CAM therapies and approaches (PAS-03-038).

Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. The overall goal of the RCE Program is to develop and maintain strong infrastructure and multifaceted research and development activities that will provide the scientific information and translational research capacity to make the next generation of therapeutics, vaccines and diagnostics against the CDC Category A-C Agents, with particular emphasis on Category A (RFA-AI-02-031).

Cooperative Reproductive Science Research Centers at Minority Institutions. The low level of involvement of minority institutions in reproductive science and the lack of sufficient training opportunities for minority scientists represent two major obstacles to developing an effective research effort aimed at addressing significant health disparities. This initiative will support the development of an enhanced research infrastructure in reproductive science at these institutions. Creating collaborations among minority institutions and other ongoing NICHD reproductive science research programs would integrate and take advantage of their respective expertise and experience (RFA-HD-00-019).

REFERENCES

NIEHS (National Institute of Environmental Health Sciences). 2000. *NIEHS Strategic Plan 2000*. [Online]. Available: http://www.niehs.nih.gov/external/plan2000/p-plan.htm [accessed December 15, 2003].

NRC (National Research Council). 1999. *From Monsoons to Microbes: Understanding the Ocean's Role in Human Health*. Washington, DC: National Academy Press.

NSF (National Science Foundation). 2000a. *Environmental Science and Engineering for the 21st Century: The Role of the National Science Foundation*. NSB 00-22. [Online]. Available at: http://www.nsf.gov/pubs/2000/nsb0022/start.htm (accessed December 15, 2003).

NSF. 2000b. Geosciences Beyond 2000: Understanding and Predicting Earth's Environment and Habitability. [Online]. Available: http://www.geo.nsf.gov/adgeo/geo2000/geo_2000_full_report.htm (accessed December 15, 2003).

F

Summary of Selected Center Program Evaluations Previously Conducted by NIH

The following summary of prior center program evaluations by the National Institutes of Health (NIH) was produced by the Institute of Medicine (IOM) staff based on publicly available copies of the referenced reports.

NATIONAL CANCER INSTITUTE

The National Cancer Institute (NCI) has supported Cancer Research Centers since at least 1961, although the Cancer Centers Program was formally conceived and established as a result of the National Cancer Act of 1971. That program has been the subject of at least three formal evaluations, which are summarized in the following three sections.

Institute of Medicine Report, "A Stronger Cancer Centers Program: Report of a Study" (1989)

In 1988 the Senate Appropriations Committee report accompanying the 1989 appropriations bill requested that NIH contract with IOM for a study on "the present state of the Cancer Centers Program and its funding and organizational needs required to fulfill the role established for cancer centers in the 1971 National Cancer Act." The Senate committee had heard increasing complaints about the flat growth in the amount of NCI funds going to cancer centers because NCI leadership apparently wanted to deemphasize the role of centers relative to other mechanisms in the national

cancer program. The IOM committee, a mixture of scientists with and without cancer center affiliations, conceded that it lacked hard evidence of the effects of cancer centers on the nature or quality of the research conducted in them and as a result relied on its collective judgment, based on expertise in biomedical research and study of existing information on cancer centers and their achievements (IOM, 1989). The report noted that scientists at the 59 centers with NCI core grants received nearly half the competitive research project grants awarded by NCI and substantial amounts of peer-reviewed funding from other NIH institutes, the National Science Foundation, and other research sponsors, and as a result, they had been involved in many of the important advances in cancer research over the preceding 20 years. They also noted that the centers were the sites for more than half the research traineeships funded by NCI and they participated extensively in the cooperative oncology groups that conducted NCI-supported clinical trials and other aspects of NCI's national cancer program. They concluded that, as a group, the centers were a valuable resource for NCI because of their interdisciplinary focus and their ability to translate research discoveries into better methods of prevention, early detection, diagnosis, and treatment.

The report's first recommendation was that the NCI director halt the slow erosion of center funding that had characterized the previous eight years. A second recommendation called for NCI to develop a systematic program plan that would ensure adequate resources, coordination with related programs, and effective scientific oversight. The committee commented in passing that, taken as a whole, the centers were involved in every aspect of the national cancer research program, but that additional incentives should be provided to encourage individual centers to broaden their research agendas. They also pointed out the disparity between NCI's support of cancer centers as research institutions and the broader role of centers intended by Congress and expected by the public. Despite the National Cancer Act of 1971's mandate for comprehensive centers that conducted not only research and research training but demonstrations of better models of care delivery, education of health care providers, public information, and community outreach programs, the cancer center core grants focused solely on support of research, and grant funds could not be used for those other purposes (IOM, 1989).

"Report of the National Cancer Institute Cancer Centers Program Review Group" (1996)

The authors of this report to the NCI director reviewed data on the history, budget, and operations of the Cancer Centers Program; heard testimony from a variety of NCI personnel and cancer center directors; and

solicited and received comments in writing from the cancer center community (NCI, 1996). They began with the assumption that "cancer centers already had demonstrated that complex research strategies are feasible, and are poised to undertake novel multidisciplinary approaches to important new research opportunities" and envisioned the review as an opportunity to recommend improvements. They recommended that only two varieties of cancer centers be recognized (comprehensive cancer research center and cancer research center) rather than three (basic, clinical, and comprehensive). This was, in part, recognition that many basic centers were also involved in translational research and that most clinical centers included a strong basic research element.

Equally important to the authors was inserting "research" into the title of the centers (i.e., cancer *research* centers), reflecting their view that research should remain the central emphasis of these centers and also the fact that core grants did not fund many of the other activities Congress and the public expected. The report took "comprehensive" to mean that the centers should perform basic, clinical, and population-based research, and it recommended that NCI provide a different mechanism for funding the education and training of biomedical researchers and health care professionals, public information services, and community service and outreach. Consistent with this view, it further recommended that centers be reviewed primarily for the quality of science and the value added by the Cancer Center core grants to the advancement of excellence in the areas of cancer research supported by NCI. The authors argued that, although a large part of a center grant supports infrastructure, these facilities should not be the primary basis of review. Rather, the cancer research that they facilitate should be the primary basis for evaluation. To that end they suggested a more stringent separation of review and program administration and more frequent use of center directors and senior faculty as reviewers. Among a number of suggestions for better use of available funds was a proposal that funding for the lowest ranked centers in each renewal cycle be phased out over a three-year period.

"Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future" (2003)

This February 2003 report by a subcommittee of the National Cancer Advisory Board was the result of a new institute director's request for advice on how the P30 (core) and P50 (specialized research) center awards might best be used to increase discovery and maximize translation into practice during he period of modest budget growth expected to follow the five-year budget doubling effort of FY1999 to FY2003 (NCAB, 2003). About half the working group's members were directors or senior staff at cancer centers, and a major source of information for the group was a

survey it conducted of P30 cancer center directors. Among other data, the survey reported the total research and operating budgets of the centers and their sources of funding. Total non-P30 research support to investigators at these centers was in excess of $1.5 billion annually, more than 10 times the amount of the P30 awards themselves. Additional income from the centers' home institution, gifts, and state and local governments totaled more than $660 million. The centers also reported having seen more than 1,100,000 newly diagnosed cancer patients over the previous five years and having enrolled nearly 30,000 patients in clinical trials in the previous year. The centers' training activities encompassed more than 9,000 basic scientists, 3,800 clinical fellows, and 3,000 oncology nurses in the previous five years. Last, the survey revealed that more than 2,500 patents had been issued to centers or center-affiliated scientists in the past five years.

NCI's P50 grants are called Specialized Programs of Research Excellence (SPOREs). They focus on organ-site-specific cancers (breast, prostate, lung, etc.) and fund not just infrastructure but specific research projects. The program began in 1992 and included 44 awards covering 11 organ sites by FY2003. The working group pointed out that this rate of growth is unsustainable, and it was also concerned about possible duplication of activities already funded by P30 grants, particularly because 41 of the 44 P50 awards were to institutions with P30 core grants. The report recommended slowing the growth of SPOREs, increasing the budget of the Cancer Center Program, and mandating that SPOREs located at a cancer center should function as a component of that center. Other suggestions for NCI included encouraging and funding centers to develop and test novel methods for disseminating new knowledge, allowing P30 grant holders to provide partial salary support to physicians with major clinical responsibilities, and developing improved and quantifiable metrics for both making individual awards and for evaluating the P30 and P50 programs.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL DISEASES

In 1997 the Director of the National Institute of Arthritis and Musculoskeletal Diseases (NIAMS) presented the NIAMS National Advisory Council with a plan for external review of the institute's center program. After approval by the Council, he appointed a 13-member working group comprised of investigators affiliated with NIAMS centers and investigators without such connections. The group developed a clear definition of issues, which were then addressed by a second working group, similar in composition to the first. Working Group II reviewed extensive background materials provided by the NIAMS staff and was briefed by representatives of other institutes on their respective center programs. A questionnaire ad-

dressing many of the issues raised by Working Group I was sent to all NIAMS center directors (N=30) and all non-center-affiliated investigators receiving more than $5 million per year in NIAMS funding (N=26). The response rate was about 50 percent for each group. The report's conclusions were as follows (NIAMS, 1997):

- Where centers had worked most effectively, it was in support of synergistic interactions between investigators and as a mechanism for support of research infrastructure, clinical research and education, epidemiology, and health services research (EEHSR).
- The P60 Multipurpose Arthritis and Musculoskeletal Disease Centers (MAMDCs) had provided economies of scale and support for pilot studies and for development of new investigators. They had made important contributions to development of the field of health services research and provided an infrastructure for communication and translation of research results to the clinical practice community. Limitations of the MAMDC Program included a focus restricted to arthritis and musculoskeletal research and an artificial requirement for combining basic science research and EEHSR components.
- In some cases, P50 Specialized Centers of Research (SCORs) had successfully provided for focused research into the problems associated with a particular disease. Often, however, this focus was limiting the scope of programs within institutions more than might be desirable, with resulting unevenness of quality among components of the SCORs.
- The P30 Skin Disease Research Centers were having a positive and important impact in the provision of essential infrastructure support for outstanding academic programs in dermatology, and the Working Group recommended that the P30 mechanism be expanded to other NIAMS program areas.
- No body of knowledge uniquely requires the centers mechanism for support. The best approach to research support regardless of subject remains the R01 research project grant. Nevertheless, it is important that the institute find other mechanisms for support of any topics crucial to the mission of NIAMS that do not attract competitive R01 applications.
- The Working Group did not believe there were critical masses of outstanding investigators necessary to justify support of MAMDCs as currently configured at more than a few institutions. The restriction of the SCOR Program to research in certain disease categories (e.g., rheumatology) was resulting in an undesirable narrowness of focus that might be obviated by centers with a broader mandate for the study of pathogenetic mechanisms.
- The Working Group concluded that the centers should be configured to promote interaction between NIAMS investigators. There should

be sufficient flexibility, including availability of several funding mechanisms (P30, P50, and P60), so that various configurations of investigators could exploit optimally their areas of expertise. Comprehensive centers of excellence existed in a small number of institutions, and continued support of such centers, utilizing the P60 mechanism, was recommended.

- Development and feasibility funds had generally proven effective in leveraging support into full project funding. Additionally, the EEHSR component of the MAMDCs appeared to have attracted significant non-NIAMS support into this area of research.
- Centers were proving particularly valuable in building and maintaining the intellectual and physical resources that serve as infrastructure for successful programs. Moreover, to the extent that centers provide an important measure of research stability and continuity, they were a valuable resource for research across the spectrum of NIAMS-related diseases.
- Every dollar so invested was not available to other funding mechanisms, particularly the R01 individual research grants program, and the Working Group believed that arthritis research was disproportionately supported through a center mechanism.
- The Working Group suggested that competing applications be grouped for review, so that relative strengths and weaknesses of applications could be directly compared. There was little enthusiasm for triaging center applications, because applications from weaker centers derive considerable benefit from thorough review and discussion of their relative strengths and weaknesses.
- Planning grants were not generally regarded as cost-effective or necessary, except perhaps modest planning grants for developing multi-institutional consortia, especially for clinical research studies. Use of the R03 funding mechanism to permit support of pilot studies by investigators in institutions or programs lacking centers was recommended for consideration.

The Working Group concluded its review by affirming the importance of the various centers programs to the mission of NIAMS. It urged continued support, albeit at a more limited level, of a variety of funding mechanisms for centers, across the breadth of NIAMS.

NATIONAL INSTITUTE OF DEAFNESS AND OTHER COMMUNICATION DISORDERS

The Work Group on Single and Multiple Project Grants was formed to provide advice to the national advisory council and director of the National Institute of Deafness and Communication Disorders (NIDCD). Its charge was to consider the benefits and drawbacks of single project (R01) grants in

contrast to multiple project (P01, P50, P60) grants and to explore the value of adding core grants (P30) to NIDCD's portfolio of extramural research mechanisms (NIDCD, 1998). Suggestions and guidance from the scientific community were requested. The NIDCD placed the charge to the Work Group, along with a series of specific questions about multiple project grants, especially centers, on its Home Page. The American Academy of Otolaryngology-Head and Neck Surgery, Association of Chemoreception Sciences, Association for Research in Otolaryngology, and American Speech-Language-Hearing Association communicated electronically with their members to provide input. In addition, the principal investigators of the 39 multiple project grants active in 1997 were solicited individually for their views.

The report recommended that NIDCD adopt a limited version of the multiple project center grant (P50) based on the following criteria:

- Projects must be *interdependent* (materials, results, data, or methodologies are shared among the projects), *interrelated* (each project must have goals and objectives that focus on the common theme), and *multidisciplinary* (subproject leaders and/or projects representing different scientific backgrounds, training, and expertise).
- The feasibility of the research proposed on any project would be significantly diminished if that project were submitted as a traditional individual research project (R01) application.

The report suggested that prospective applicants be asked to explain in a letter of intent exactly how their proposed applications meet these criteria.

The Work Group also recommended that NIDCD initiate a core grant (P30) program to complement the P50 multiple project center grants program. On the other hand, its analysis of the five existing P60 multipurpose centers mandated by law led them to recommend that an alternative funding mechanism for the continuing education and information dissemination activities supported by the P60 mechanism be explored. Finally, they recommended that NIDCD be included as a participant in the NIH Interactive Research Project Grant (IRPG) Program. The IRPG Program provides for the coordinated submission of two or more applications for related traditional research project grants (R01) on related topics, with a formalized agreement to collaborate in specific ways to enhance the achievement of the goals on all projects. This would require that NIDCD develop a rapid review capability to determine the additional resources, if any, that would be required to optimize performance for those collaborating grantees, assuming that both are rated highly by their respective study sections at the Center for Scientific Review.

OFFICE OF AIDS RESEARCH

The Centers for AIDS Research (CFAR) program was established in 1988 by the Office of AIDS Research (OAR) Advisory Council to provide an environment for multidisciplinary collaborations by basic, clinical, epidemiological, and behavioral scientists. In 1995 the CFAR program was evaluated as part of a comprehensive review by the NIH AIDS Research Program Evaluation Working Group, known as the "Levine Report" (OAR, 1996).[1] The Levine Report recommended strengthening CFARs to promote multidisciplinary AIDS research by increasing the funding for the program. This resulted in the doubling of the CFAR program and the participation of five additional institutes beyond the National Institute of Allergy and Infectious Diseases.

In 1999, in view of the substantial changes that had been introduced, OAR decided to conduct a review that would focus exclusively on the structure of the CFAR program, to assess its successes and identify needed course corrections. A focus group of external consultants was convened to conduct such a review. The focus group was notable for its inclusion not only of scientists representing a broad range of disciplines and experience with research centers (none from CFARs), but also of scientists from Europe and Africa and a nonscientist member of the AIDS Vaccine Advocacy Coalition. They were joined at the group's single face-to-face meeting by discussants who were engaged in CFAR-related research activities, as well as two CFAR directors.

The ensuing "Report of the Focus Group to Review the Centers for AIDS Research (CFAR) Program" concluded that the CFAR program had been successful in fostering collaboration between existing research programs related to HIV and AIDS, had promoted multidisciplinary approaches to AIDS/HIV-related problems, and had provided added value beyond the sum of the individual parts (OAR, 1999). It cited examples where CFARs had successfully leveraged developmental funds to increase investigator-initiated R01 funding among junior faculty members; enhanced faculty recruitment; refocused existing faculty not currently engaged in AIDS research on HIV-related issues; and generated significant local institutional support for the center program. It recommended that the size and overall proportion of the NIH AIDS budget devoted to CFARs should be increased (but in a stepwise manner over three years to minimize the impact on funding for R01s). It also emphasized that sustained growth of the program, particularly in terms of a percentage of the overall budget, should be contingent on improved outcome measures that can show added value of the CFAR program beyond funding of independent awards.

[1]The report was named after its chair, Arnold J. Levine, of Princeton University.

The authors conceded that much of the value of a center program is intangible, qualitative, and anecdotal, but felt that more effort should be placed on objectifying the measurement of added value. Examples of possible measures of the impact of a center program included lists of interdisciplinary manuscripts; new grant support for faculty previously funded by pilot projects; evidence of enhancement of existing programs; the use of core facilities; the number of protocols started within a single institution; other evidence of translational work, such as applications for patents; and evidence of leveraging pilot studies into R01 funding or CFAR support into institutional support. The group also felt that more emphasis should be placed on promoting the development of future investigators, either through support and mentoring of junior faculty or attraction of established investigators into the field of HIV-related research.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

The mission of the Demographic and Behavioral Sciences Branch (DBSB) of the National Institute of Child Health and Human Development (NICHD) is to foster research on the processes that determine population size, growth, composition and distribution, and on the determinants and consequences of those processes. DBSB maintains a network of Population Research Centers that provide core support (P30 awards) for research projects relevant to the DBSB mission at leading universities and research centers throughout the United States. The Population Research Centers Program had begun in the early 1970s, and in 1999 DBSB staff decided that a review of the program was in order. The review was not intended to assess the merit or productivity of specific centers, but to review the way in which NICHD had shaped the program over the last few decades and to explore strategies for the future.

DBSB recruited six scientific experts to assist in conducting the evaluation, two of whom were affiliated with institutions receiving NICHD center support. The scientists reviewed data summarizing the fiscal and scientific scope of the Centers Program as it existed currently; interviewed key constituencies concerning the existing and potential functions of infrastructure support in the population sciences; reviewed comments received by the branch regarding the Centers Program; and reviewed information on alternative models of structuring infrastructure support programs in the behavioral and social sciences. A request for comments was posted on the branch's webpage, which resulted in 77 replies. The consulting scientists spoke with colleagues in the field, and NIH provided historical data about the grant submissions and funding histories of both NICHD-funded and nonfunded population centers. Based on these data, the consultants assisted the branch

in developing recommendations for adapting and changing the program to meet future scientific needs.

The "Report of the Demographic and Behavioral Sciences Branch Population Centers Review" recommended that NICHD continue to support infrastructure for population research at about the same level as present, allowing for inflation (NICHD, 1999). It cited data showing that institutions with NICHD-funded centers submitted more applications to NICHD and had higher success rates than non-NICHD-funded centers; NICHD-funded centers provided support for an average of 32 individual research projects at each site; and centers were highly successful in leveraging substantial additional funds for both research and infrastructure (93 percent of center funds came from sources other than the P30 grant). The authors nevertheless called for increased flexibility in the way funds could be expended at the center level. For example, they called for seed money programs to quickly provide money for pilot projects, giving centers permission to support noncenter scientists doing relevant population research; and a stronger link to graduate training. They came out strongly against "sunset" rules, instead offering several suggestions to improve competition in the application/renewal process.

A unique feature of the report was a concluding section in which staff outlined plans for implementing the report's suggested changes. In short, staff proposed that center core grants be phased out in favor of R24 research resource-related grants. The R24 has many of the characteristics of the traditional center grants, e.g., support of infrastructure to support a portfolio of research in an institution. However, according to staff, the R24 would provide more flexibility than the P30 grant, enabling centers to pursue scientific opportunities at the boundary between traditional population research and allied fields and to facilitate partnerships among center personnel and collaborators in other institutions and between the center and complementary institutions around the world. Eligibility for an R24 infrastructure grant depends on the existence of a center or other identifiable administrative unit at the applicant institution, but applicants would be able to request support for:

- Core services and facilities similar to those found in traditional P30 grants;
- Developmental infrastructure (e.g., seed grants, faculty development, technological specialists, and planning workshops);
- Translational cores to provide support for public-use access to large-scale data collection projects housed in the center, and/or outreach efforts to elucidate the clinical or public policy implications of work ongoing within the center;

- Cooperative research partnerships with colleagues in other institutions and joint ventures with other institutions to provide research services to center researchers; and
- Research projects similar to R01 projects.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Institute (NHLBI) initiated SCOR programs in 1971 to encourage research to translate basic science findings to the clinic. SCOR grants require both basic and clinical research projects focused on diseases and clinical problems relevant to the mission of the institute. The interactions between the basic and clinical projects are intended to enhance transfer of fundamental research findings to the clinical setting and to help focus fundamental research investigations on issues of major clinical importance. By FY2001 NHLBI had 14 different SCOR programs, each supporting several centers.

In 1993 NHLBI established a process of inviting extramural experts to conduct a formal evaluation of each SCOR program early in its second five-year funding period to advise the institute on continued relevance and future directions. Unless "extraordinarily important reasons" to continue a specific SCOR program are identified, a sunset provision limits the program to 10 years of continuous funding (Lenfant, 2002). Two reviews in late 2000 and early 2001 noted excellent scientific productivity in the two SCOR programs they evaluated, but they both noted that direct contributions to clinical care were not clear and there was little evidence of productive collaborations between basic and clinical investigators. These comments raised concerns that the SCOR mechanism may not be fulfilling its intended translational research function, and thus it may not be distinguishable in practice from the P01 program project grant mechanism. In response to these findings, the NHLBI director appointed a SCOR "reinvention committee" of extramural program staff, which was charged with evaluating the strengths and weaknesses of the SCOR mechanism and recommending ways to enhance the clinical focus and utility in SCOR programs.

The "Report from the Committee to Redefine the Specialized Centers of Research Programs" was completed in September 2001 (NHLBI, 2001). In it, the committee agreed unanimously that the SCOR program offers a unique mechanism for producing collaboration between basic and clinical researchers that would otherwise be unlikely to occur. Furthermore, the SCOR program provides an excellent tool to further NHLBI's goal of translating bench findings to the bedside, and SCOR centers are a natural venue for training both basic scientists and clinicians in clinical research. They also agreed that clinically relevant questions should be the central

theme in the next iteration of SCOR awards, despite the fact that the clinical questions posed in past SCOR programs have not been as well developed as the basic science research. The report's recommendations focus on how to change that.

First was a recommendation to begin with a new title that emphasizes the centrality of clinical research—Specialized Centers of Clinically Oriented Research (SCCOR). The committee recommended that the number of clinical projects in each SCCOR must be greater than or equal to the number of basic science projects (only a single clinical project was required in SCORs regardless of the number of basic projects).

The committee recognized that expanded clinical research would require more and different types of infrastructure support and made several suggestions along those lines. They recommended that the Request for Applications (RFA) stipulate that the resources represented by cores and any materials developed in them (e.g., biological specimens) should be shared widely within the SCCOR program (i.e., with grantees at other institutions). They also suggested that each SCCOR program carefully consider the possible benefits of supporting a clinical core to serve all grantees in the SCCOR, in which case a single clinical core would be chosen from among all grantees. The committee made several suggestions designed to provide more weight to clinical research in the review of individual applications, recommended that the budget cap for individual awards be raised even if it meant fewer awards, and supported the five-year award length and the outside review and sunset provisions of the SCOR programs.

NATIONAL INSTITUTE ON AGING

In 1984 Congress directed the National Institute on Aging (NIA) to foster further research on Alzheimer's disease, and NIA responded by initiating the Alzheimer's Disease Center (ADC) program, which now includes 17 Alzheimer's Disease Research Centers (ADRCs) and 12 Alzheimer's Disease Core Centers (ADCCs). In January 2003 NIA issued an RFA inviting applications for support of ADRCs.[2] The RFA was issued in anticipation of funding nine new and/or competing renewal ADRC grants in FY2004, but in preparing the RFA the NIA sought input from scientists both inside and outside of the existing centers on what had worked well during the first 20 years of the ADCC program and what had not, and on whether the configuration of the centers program is the best one for the foreseeable future. Suggestions for changes that would improve center op-

[2]RFA-AG-03-006.

erations were discussed in a meeting of all current center directors and NIA staff held in May 2001. A second, smaller meeting garnered the views of outside scientific experts who did not have primary affiliations with any of the centers. The committee of outside experts concluded that the ADC program has been very successful, but suggested that some constructive changes could be made in the program to improve Alzheimer's disease research.

Four main recommendations were put forth in the committee's report (NIA, 2002). The first was to give the centers greater program flexibility to take better advantage of local strengths, interests, and expertise. For example, it was suggested that centers might enroll and follow special patient populations rather than using only clinic populations as has been required up to now. Another example was that centers be allowed to purchase some required services, e.g., postmortem neuropathology or educational programs, from another center or an outside organization such as the Alzheimer's Association.

A second recommendation was to accelerate standardized clinical data collection across ADCs. Although each center would be encouraged to continue collecting data needed for local research interests, additional standardized neuropsychological and neurological data should be collected by all centers and transmitted to the National Alzheimer's Coordinating Center (NACC) where data from all centers will be pooled for studies requiring large sample sizes.

A similar suggestion resulted in the third recommendation, which was that the program promote better use and increased sharing of tissue and data resources among the centers and the general scientific community. The committee suggested expanding the National Alzheimer's Cell Repository located at Indiana University to increase its capacity to bank cell lines, DNA, and serum from the centers as well as other sources. Another suggestion was that increased use of the frozen or fixed postmortem brain tissue collected and stored at all centers for collaborative studies coordinated by NACC using pooled samples and data could increase statistical power.

A fourth recommendation was to decrease the emphasis on late-stage Alzheimer's disease in favor of more research on the transition from normal aging to mild cognitive impairment and to full-blown Alzheimer's disease as well as to comparisons to other neurodegenerative diseases. The recommendations of the external review committee were incorporated in the 2003 RFA for ADRCs.

NATIONAL INSTITUTE OF NURSING RESEARCH

The National Institute of Nursing Research (NINR) uses two types of center awards to support university-based research centers. Nine P30 core

grants support interdisciplinary, collaborative nursing research programs at established research institutions, and nine P20 exploratory center grants support nursing schools in the process of developing their research programs. Each center has a broad topic or area of research focus, with little overlap across the 18 centers. Examples of research areas include vulnerable populations, chronic disorders, symptom management, health promotion, and injury mechanisms. All NINR-funded centers are required to have evaluation plans as part of their application, and the annual meeting of center directors in 2001 focused on these program evaluations, specifically whether the centers are meeting their stated objectives and goals and what they have accomplished that they would not have been able to do without center awards. Those discussions were subsequently reported to the NINR Advisory Council (NINR, 2002).

The center directors identified a range of benefits of the centers program, including:

- Enabling nurse researchers to move from relatively small, exploratory studies to more sophisticated "big science" intervention studies;
- Defining new areas of nursing research;
- Recruiting new faculty within a particular research area and recruiting graduate students and postdoctoral fellows;
- Using the centers as a research dissemination vehicle;
- Developing new evidence-based practice models;
- Bringing the school of nursing into the larger campus or university by bridging gaps between disciplines, departments, and faculty;
- Giving faculty members a vehicle to take risks that previously might not have been feasible;
- Strengthening and expanding community linkages; and
- Leveraging more research funding from the university.

Challenges identified by the center directors were:

- Devising adequate mentorship strategies and establishing a group of core mentors. For P20s, the key issue was mentoring developing investigators; for the P30s, key issues were mentoring for midcareer researchers and sustained leadership.
- Accruing and maintaining adequate resources, even though the centers are receiving NINR and other support.
- Allowing adequate time to achieve the stated goals. For P20s in particular, the three-year lifespan may not be sufficient to develop the research base and infrastructure needed to apply for a P30.
- Sustaining leadership and a core faculty within the centers.

NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

The director of the National Center for Complementary and Alternative Medicine (NCCAM) convened a panel of outside experts in 2002 to review the NCCAM research center program, which was approaching the end of the initial five-year funding cycle. The panel was asked to examine NCCAM's system of research centers and determine whether modifications to their present organization and funding were merited. In particular, the panel was asked to consider the role that research centers have played in advancing NCCAM's mission and how that role should change in the future; important characteristics of future centers; and the most suitable funding mechanisms for various types of centers (NCCAM, 2002).

The earliest NIH-funded complementary and alternative medicine (CAM) centers were expected to emphasize outreach to researchers, academic institutions, and the public in addition to conducting research. Each of the centers was to provide technical assistance to investigators, develop bibliographic resources, foster connections between experienced investigators from conventional medicine and those from the CAM community, and establish linkages among academic centers studying alternative medicine.

Many of the 10 U24 "exploratory centers" found it difficult to meet these ambitious goals, and as a result, when the U24 CAM centers reached the end of their funding cycles, the goals for the center program were revised and a different funding mechanism was adopted. NCCAM's present-day Research Centers Program employs P50 specialized center of research grants, which provide more funds ($1.5 million annually versus the $450,000 allotted to the earlier U24 centers) and more focus (centers are expected to carry out three or four R01-like research projects that undergo NIH peer review, conduct pilot research projects, and provide continuing opportunities for research career development).

The panel found that, several years into their missions, the current NCCAM research centers had clearly played a role in establishing the visibility and credibility of CAM research, building research infrastructure, and drawing investigators into the field. For these reasons, panel members soundly endorsed the continuation of a vigorous NCCAM Research Centers Program. Nevertheless, the panel also pointed out that the current P50 research centers had not yet developed a consistent record of hypothesis-driven research and publication. Accordingly, the panel members urged that future NCCAM research centers be structured to focus on two or three of the following:

- A particular disease or class of diseases treated by CAM;
- A specific group of CAM therapies or treatment approaches; and

- Mechanisms (or processes) of action of CAM therapies and approaches.

The panel also suggested that there may be scientific and fiscal advantages to using funding mechanisms other than P50 grants that dominated NCCAM's current research centers portfolio. Although it did not stipulate specific funding mechanisms, the panel encouraged NCCAM to select types of awards that encourage investigator autonomy wherever possible. In response, NCCAM restructured its center program to consist of three activities, "each designed to meet a different need": Centers of Excellence for Research on Complementary and Alternative Medicine funded by P01 grants; Developmental Centers for Research on Complementary and Alternative Medicine funded by U19 cooperative agreements; and International Centers for Research on Complementary and Alternative Medicine funded by R21 grants.[3]

Additional panel recommendations for future NCCAM centers included:

- More basic science research in CAM;
- Opportunities for peer-reviewed pilot research projects;
- Extending research support and infrastructure to noncenter investigators conducting related research elsewhere;
- Standardized treatments and therapeutic approaches for large-scale clinical trials;
- Career development opportunities for conventional and CAM clinicians who have completed their clinical training, especially junior faculty; and
- Cost-effectiveness or health services research.

Finally, panelists recommended that NCCAM carefully monitor the accomplishments of future centers and continue to support only those with exemplary research records.

REFERENCES

IOM (Institute of Medicine). 1989. *A Stronger Cancer Centers Program: Report of a Study*. Washington, DC: National Academy Press.

Lenfant C. 2002. Strengthening commitment to clinical research: The National Heart, Lung, and Blood Institute's Specialized Centers of Research program. *Circulation* 105(4):400-401. [Online]. Available: http://www.nhlbi..nih.gov/funding/fromdir/circ-1-02.htm [accessed December 15, 2003].

[3]PAS-03-038.

NCAB (National Cancer Advisory Board). 2003. *Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future*. Report of the National Cancer Advisory Board Ad Hoc P30/P50 Working Group. [Online]. Available: http://deainfo.nci.nih.gov/ADVISORY/ncab/p30-p50/P30-P50final12feb03.pdf [accessed December 15, 2003].

NCI (National Cancer Institute). 1996. Report of the National Cancer Institute Cancer Centers Program Review Group. Bethesda, MD: National Cancer Institute

NCCAM (National Center for Complementary and Alternative Medicine). 2002. *NCCAM Research Centers Program Expert Panel Review*. [Online]. Available: http://nccam.nih.gov/about/plans/centers/report.pdfx [accessed January 8, 2003].

NHLBI (National Heart, Lung, and Blood Institute) 2001. *Report from the Committee to Redefine the Specialized Centers of Research Programs*. [Online]. Available: http://www.nhlbi.nih.gov/funding/scor_report.pdf [accessed December 15, 2003].

NIA (National Institute on Aging). 2002. *Report of the Alzheimer's Disease Centers External Advisory Meeting*. [Online]. Available: http://www.nia.nih.gov/news/alzadvmtg.htm [accessed December 15, 2003].

NIAMS (National Institute of Arthritis and Musculoskeletal and Skin Diseases). 1997. *Executive Summary, Report to the Institute Director of the Centers Working Group II*. [Online]. Available: http://www.niams.nih.gov/ne/reports/sci_wrk/1997/cenrptfn.htm [accessed December 15, 2003].

NICHD (National Institute of Child Health and Human Development). 1999. "Report of the Demographic and Behavioral Sciences Branch Population Centers Review." [Online.] Available: http://www.nichd.nih.gov/about/cpr/dbs/pubs/report.pdf [accessed December 15, 2003].

NIDCD (National Institute on Deafness and Other Communication Disorders. 1998. *Report of the Work Group on Single and Multiple Project Grants Report*. Bethesda, MD: National Institute on Deafness and Other Communication Disorders.

NINR (National Advisory Council for Nursing Research). 2002. *Minutes of the Advisory Council of May 21-22, 2002*. [Online]. Available: http://www.nih.gov/ninr/about/may_min02.pdf [accessed December 15, 2003].

OAR (Office of AIDS Research). 1996. *Report of the NIH AIDS Research Program Evaluation Working Group of the Office of AIDS Research Advisory Committee* ("Levine Report"). [Online]. Available: http://www.nih.gov/od/oar/public/pubs/levine.pdf [accessed December 15, 2003].

OAR. 1999. *Report to the Director, Office of AIDS Research, of the Focus Group to Review the Centers for AIDS Research (CFAR) Program*. [Online]. Available: http://www.nih.gov/od/oar/public/CFARrpt090899.pdf [accessed December 15, 2003].