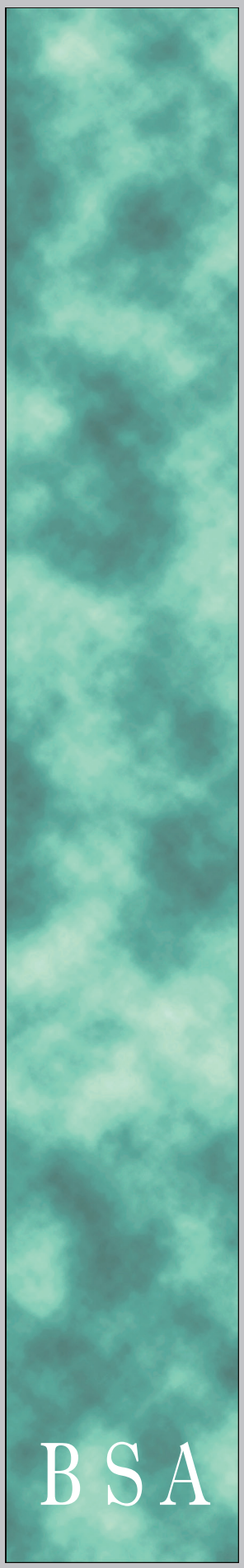

NATIONAL CANCER INSTITUTE

Orientation

for the

Board of Scientific Advisors

National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Orientation

for the

Board of Scientific Advisors

National Cancer Institute
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FOREWORD

Congratulations on your recent appointment to the Board of Scientific Advisors (BSA). As you join this distinguished panel, we could not be more honored to have you working with the National Cancer Institute (NCI).

The primary task of the BSA is to advise the Director of the NCI and the Director of each NCI Division/Office on a wide variety of matters concerning scientific program policy as well as progress and future direction of extramural research programs of each of the Divisions. This includes the concept review of requests for applications for grants and cooperative agreements, and requests for proposals for research and development (R&D) contracts. This briefing document has been prepared to provide new members of the BSA with an overview of the mission, history, and activities of the National Institutes of Health (NIH) and the NCI.

The first section presents the NCI in the context of the total NIH organization. It includes budgetary information, cites current legislative statutes, and describes organizational structure, program disciplines, and mechanisms of funding used by the NCI. It also delineates the roles of those committees that advise the NCI in the conduct of its activities.

The second section describes the process used in the review of grant and cooperative agreement applications and contract proposals. It outlines the initial review procedures followed by the Center for Scientific Review (CSR) and the review groups of the NCI.

The subsequent three sections focus on the responsibilities of the BSA, including a summary of the BSA charter, selection of the appropriate award mechanism, and the NCI concept review process, including the role of the BSA. In previously held BSA Listens sessions in conjunction with NCI staff, the BSA played an important role in discussions held at national meetings. As a result, a summary of frequently asked questions from these past sessions has been provided in this orientation. Finally, a brief discussion of ethics and conflict of interest issues is included as a reference.

We are pleased to provide you with this BSA Orientation Book and hope you will refer to it often in fulfilling your responsibilities as a member of the BSA.

Paulette S. Gray, Ph.D.
Director
Division of Extramural Activities
and
Executive Secretary
Board of Scientific Advisors
National Cancer Institute

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HHS MISSION AND ORGANIZATION

The mission of the Department of Health and Human Services (HHS) is to enhance the health and well being of Americans by providing for effective health and human services and by fostering strong, sustained advances in the sciences underlying medicine, public health, and social services. The HHS consists of the Office of the Secretary, which provides leadership; the Program Support Center, which provides centralized administrative support; and 12 operating divisions, which manage more than 300 health-related programs. These operating divisions are:

Administration for Children and Families (ACF)

Administration on Aging (AoA)

Agency for Healthcare Research and Quality (AHRQ)

Agency for Toxic Substances and Disease Registry (ATSDR)

Centers for Disease Control and Prevention (CDC)

Centers for Medicare and Medicaid Services (CMS) [formerly the Health Care Financing Administration (HCFA)]

Food and Drug Administration (FDA)

Health Resources and Services Administration (HRSA)

Indian Health Service (IHS)

National Institutes of Health (NIH)

Program Support Center (PSC)

Substance Abuse and Mental Health Services Administration (SAMHSA)

The ACF is responsible for temporary assistance to needy families; children's welfare, care and support; disabilities programs; and other services. The AoA serves the elderly. The CMS manages health insurance programs, while the PSC provides products and services to the HHS and other Federal agencies. The NIH, AHRQ, ATSDR, CDC, FDA, HRSA, IHS, and SAMHSA are all devoted to public health and compose the Public Health Service (PHS) (see Exhibit I)

THE NATIONAL INSTITUTES OF HEALTH

Mission, Organization, and History

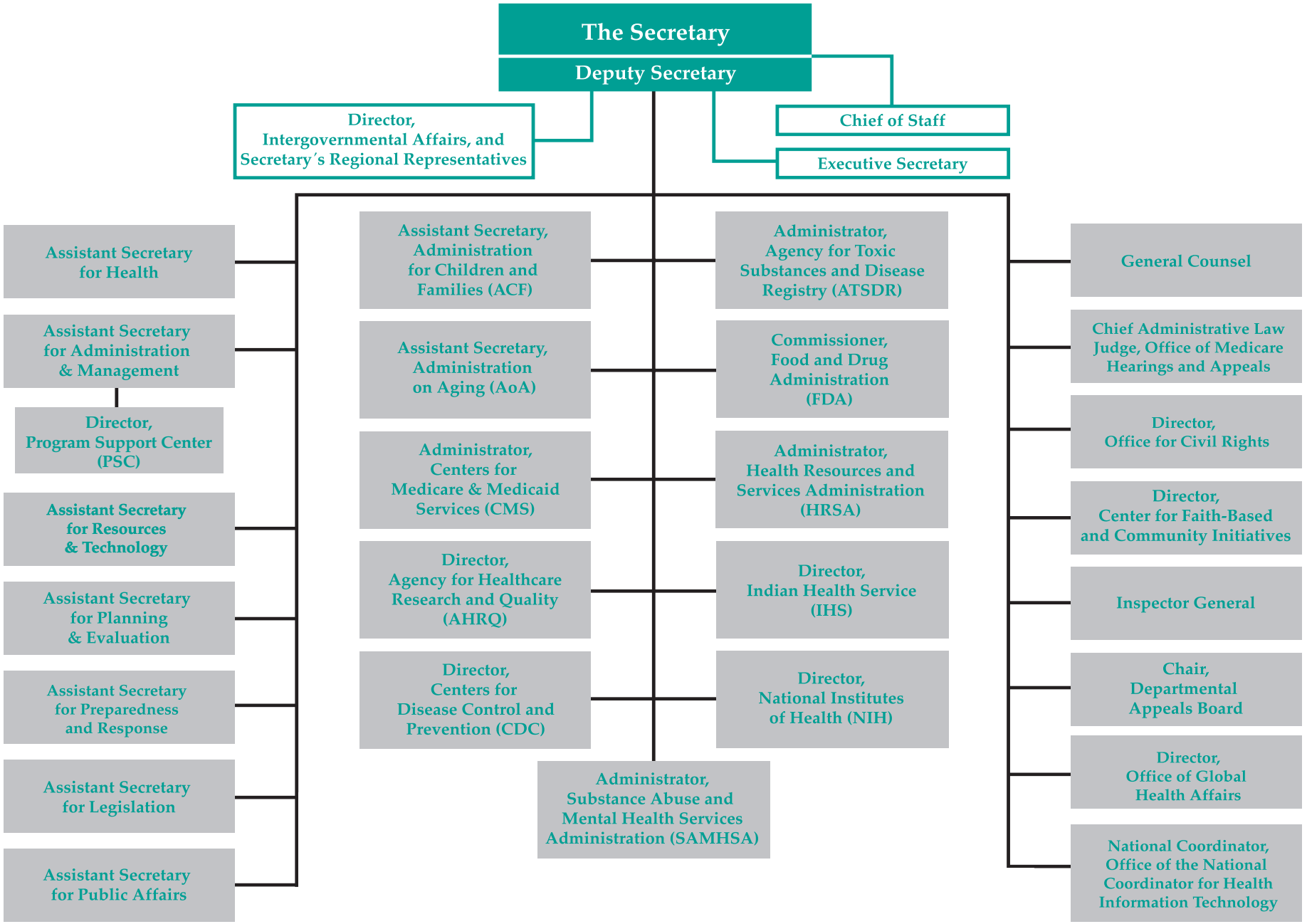
NIH's mission is to uncover new knowledge that will lead to better health for everyone. The NIH works toward that mission by conducting research in its own laboratories; supporting the research of non-Federal scientists in universities, medical schools, hospitals, and research institutions throughout the country and abroad; helping to train research investigators; and fostering communication of medical information. NIH's budget has grown from $300 in 1887, when the NIH was a one-room Laboratory of Hygiene, to more than $31 billion in 2010 (see Exhibit II). The NIH is composed of the Office of the Director, 19 Institutes, 7 Centers (four of which have funding authority), and the National Library of Medicine; it has 75 buildings located on more than 300 acres in Bethesda, Maryland. An organizational chart for the NIH is presented in Exhibit III. Exhibit IV is a guide to the Bethesda campus.

Overview of NIH History

NIH is a component of the Public Health Service (PHS) of HHS. The PHS traces its origin to "An Act for the Relief of Sick and Disabled Seamen" of 1798 (Stat. L. 604), which authorized the establishment of marine hospitals for the care of American merchant seamen. In 1912, the Public Health and Marine Hospital Service became the Public Health Service.

The actual forerunner of the National Institutes of Health was established in 1887 as the Laboratory of Hygiene, located at the Marine Hospital of Staten Island, New York. In 1930, this laboratory was renamed the National Institute of Health. The first of the present Institutes, the National Cancer Institute (NCI), was established in 1937 by an act of Congress. In 1938, the National Advisory Cancer Council approved the first awards for research training fellowships in cancer research. In 1948, the National Heart Institute was established, and the National Institute of Health

Exhibit I. Department of Health and Human Services



became the National Institutes of Health (NIH). During the years 1949-2001, NIH expanded to include 27 Institutes and Centers. The current NIH Institutes, in order of their establishment, are:

1798 President John Adams signed "an Act for the relief of sick and disabled Seamen," which led to the establishment of the Marine Hospital Service.

1803 The first permanent Marine Hospital was authorized to be built in Boston, Massachusetts.

1836 The Library of the Office of Surgeon General of the Army was established.

1870 President Grant signed a law establishing a "Bureau of the U.S. Marine Hospital Service" within the Treasury Department. This Bureau, headed by a Supervising Surgeon (later Surgeon General), was given central control over the hospitals.

1887 The Laboratory of Hygiene at the Marine Hospital in Staten Island, New York, was established for research in cholera and other infectious diseases.

1891 The Laboratory of Hygiene was redesignated the Hygienic Laboratory and moved from Staten Island to the Marine Hospital Service headquarters in Washington, DC.

1902 The Advisory Board for Hygienic Laboratory was established; later became the National Advisory Health Council. Act of Congress changed name of Marine Hospital Service to the Public Health and Marine Hospital Service. Hygienic Laboratory was authorized by Congress to regulate laboratories that produced "biologicals." The Hygienic Laboratory was expanded to four divisions: Bacteriology and Pathology, Chemistry, Pharmacology, and Zoology.

1912 The Public Health and Marine Hospital Service was renamed Public Health Service (PHS).

1922 The Library of the Office of Surgeon General was renamed Army Medical Library.

1930 The Hygienic Laboratory was renamed the National Institute of Health (NIH). Congress authorized construction of two buildings for the NIH and a system of fellowships.

1937 Congress authorized the establishment of the National Cancer Institute (NCI) and the awarding of research grants. Rocky Mountain Laboratory became part of the NIH. The National Advisory Cancer Council held its first meeting.

1938 The NIH was moved to land donated by Mr. and Mrs. Luke I. Wilson, located in Bethesda, Maryland. Cornerstone for Shannon Building was laid.

1939 The Public Health Service (PHS) became part of a newly created Federal Security Agency; until that time, it was part of the Treasury Department.

1946 The Division of Research Grants was established to process NIH grants and fellowships to non-Federal institutions and scientists. (Originally established as the Research Grants Office, it was renamed the Research Grants Division and, finally, the Division of Research Grants.)

1948 The National Heart Institute was authorized. Several laboratories (including Rocky Mountain Laboratory) were regrouped to form the National Microbiological Institute. The Experimental Biology and Medicine Institute and the National Institute of Dental Research were established. The National Institute of Health became the National Institutes of Health.

1949 The Mental Hygiene Program of the PHS was transferred to the NIH and expanded to become the National Institute of Mental Health.

1950 The "Omnibus Medical Research Act" authorized the establishment of the National Institute of Neurological Diseases and Blindness, as well as the National Institute of Arthritis and Metabolic Diseases. The latter absorbed the Experimental Biology and Medicine Institute.

Exhibit II. NIH FY2008-2010 Funding*

INSTITUTE/ CENTER	FUNDING (Dollars in Thousands)		
	2008	2009	2010
NCI	4,830,647	4,968,973	5,103,388
NHLBI	2,938,470	3,015,689	3,096,916
NIDCR	391,778	402,652	413,236
NIDDK	1,864,945	1,911,338	1,808,100
NINDS	1,552,113	1,593,344	1,636,371
NIAID	4,288,585	4,702,572	4,818,275
NIGMS	1,946,104	1,997,801	2,051,798
NICHD	1,261,381	1,294,894	1,329,528
NEI	670,664	688,480	707,036
NIEHS	723,215	740,894	689,781
NIA	1,052,830	1,080,796	1,110,229
NIAMS	511,291	524,872	539,082
NIDCD	396,234	407,259	418,833
NIMH	1,412,951	1,450,491	1,489,372
NIDA	1,006,022	1,032,759	1,059,848
NIAAA	438,579	450,230	462,346
NINR	138,207	141,879	145,660
NHGRI	489,368	502,367	516,028
NIBIB	300,233	308,208	316,582
NCRR	1,155,560	1,226,263	1,268,896
NCCAM	122,224	125,471	128,844
NCMHD	200,630	205,959	211,572
FIC	66,912	68,691	70,051
NLM	322,667	330,771	339,716
OD	1,111,735	1,246,864	1,177,300
B&F	118,966	125,581	100,000
TOTAL	29,312,311	30,545,098	31,008,788

*Source: *NIH Almanac*, 2010.

1953 The PHS became part of the newly created Department of Health, Education, and Welfare. The Clinical Center opened.

1955 The National Microbiological Institute was renamed National Institute of Allergy and Infectious Diseases. The Laboratory of Biologics Control was renamed the Division of Biologics Standards. The Division of Research Services was created.

1956 The Armed Forces Medical Library was renamed the National Library of Medicine (NLM) and placed in the PHS.

1957 The Center for Aging Research was established.

1958 The Division of General Medical Sciences was created. The Center for Aging Research was transferred from the National Heart Institute to the Division of General Medical Sciences.

1961 The Center for Research in Child Health was established within the Division of General Medical Sciences.

1962 The NLM was moved to the NIH campus.

1963 The Division of General Medical Sciences was renamed the National Institute of General Medical Sciences (NIGMS). The National Institute of Child Health and Human Development (NICHD) was created.

1966 The Division of Environmental Health Sciences was created.

1967 The National Institute of Mental Health was separated from the NIH and became a separate bureau of the PHS.

1968 The John E. Fogarty International Center (FIC) for Advanced Study in the Health Sciences was created. The Bureau of Health Manpower and the NLM became part of the NIH. The National Eye Institute (NEI) was created. The National Institute of Neurological Diseases and Blindness was renamed

Exhibit III. National Institutes of Health

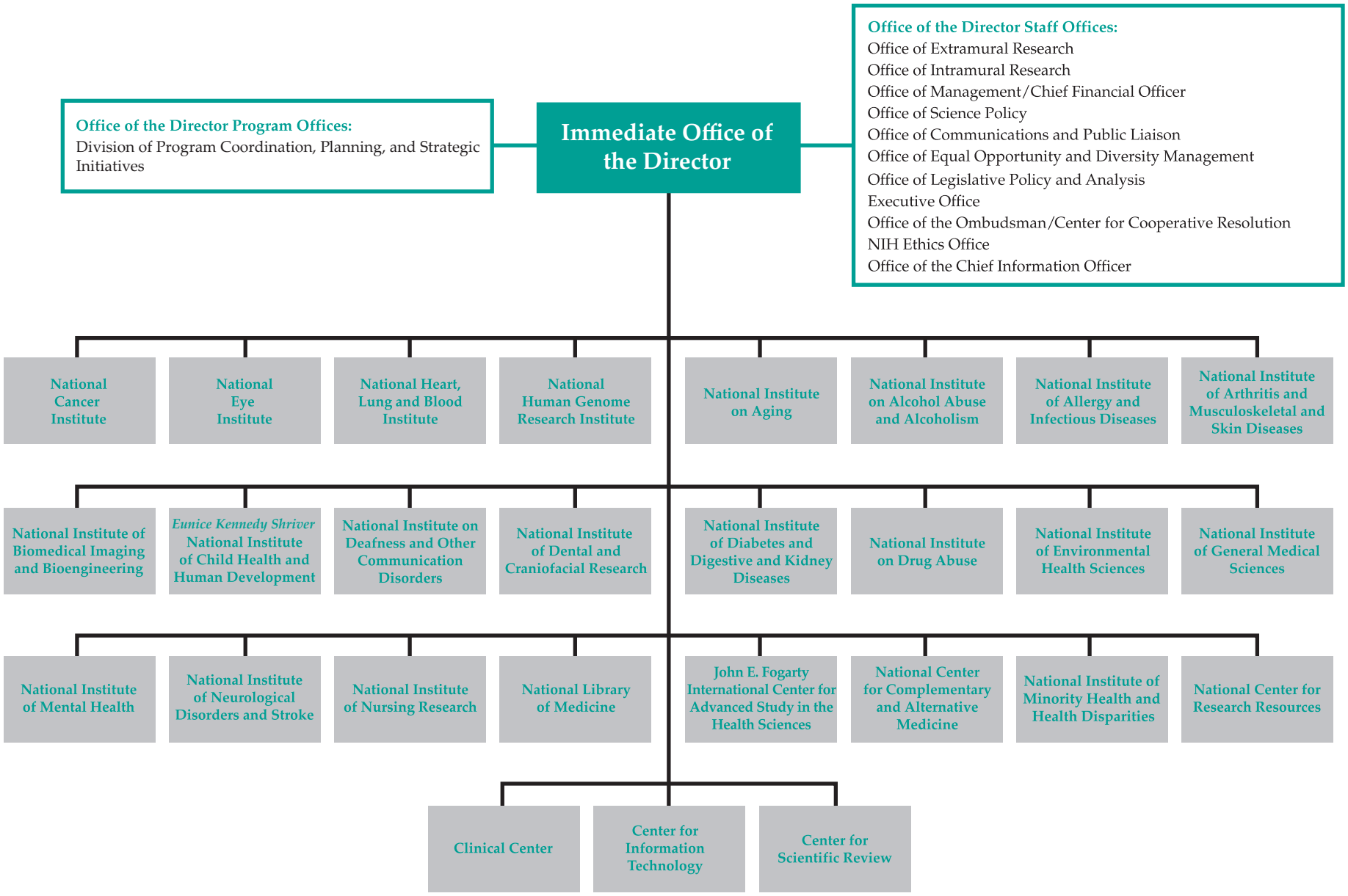
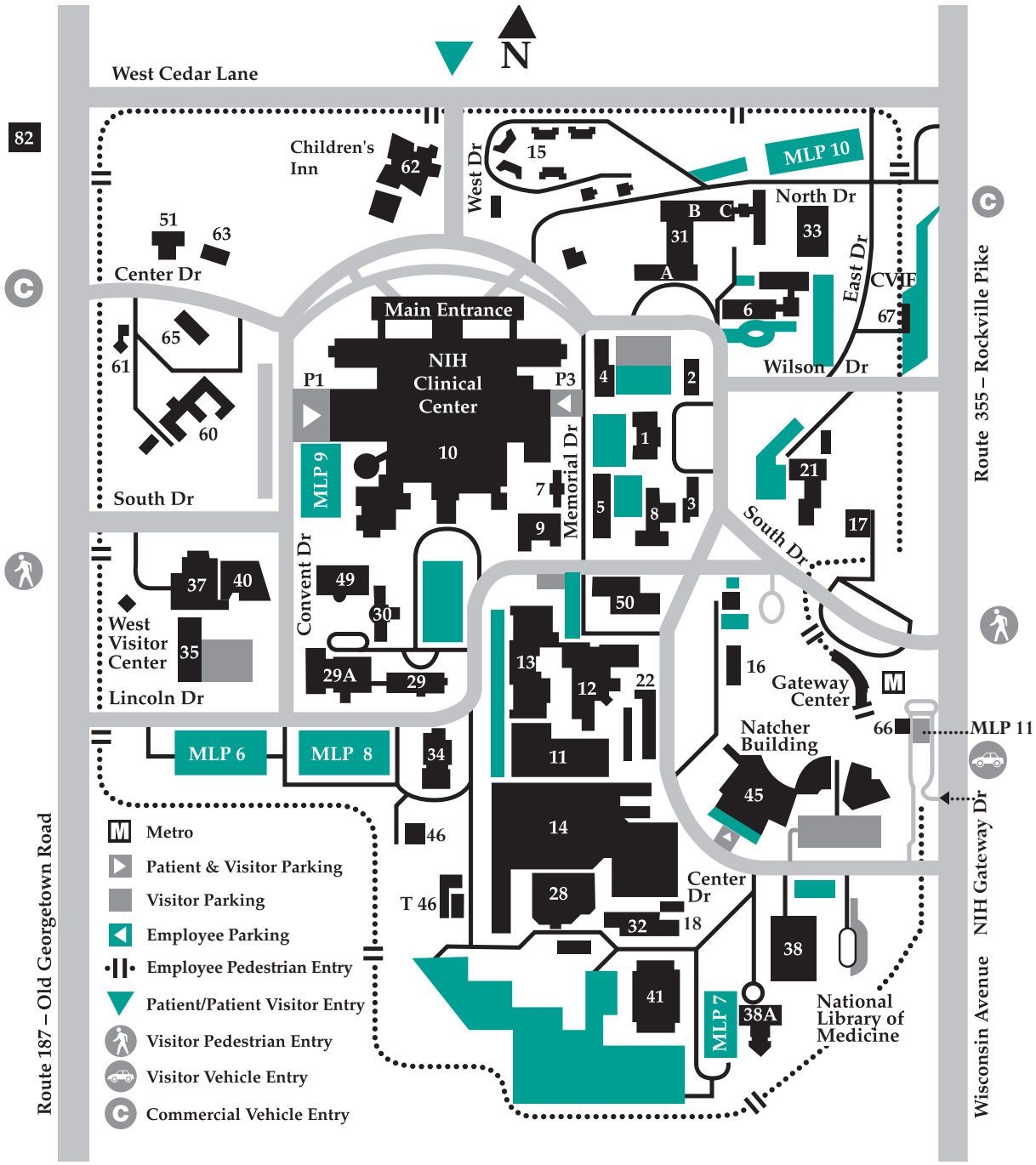


Exhibit IV. NIH Facilities Map



Building Key

Building 1	James Shannon Building (NIH Administration)
Building 10	Warren Grant Magnuson Clinical Center; Mark Hatfield Clinical Research Center
Building 11	Central Utility Plant
Building 13	Engineering Services
Building 14	Office of Research Facilities
Building 16	Stone House
Building 31	Claude D. Pepper Building (General Office Building)
Building 36	Lowell P. Weicker Building
Building 38	National Library of Medicine
Building 38A	Lister Hill
Building 40	Vaccine Research Center
Building 45	Natcher Building and Conference Center
Building 49	Sylvio Conte Building
Building 50	Stokes Laboratories
Building 60	Mary Woodard Lasker Center
Building 62	The Children's Inn at NIH
Blue, Parking Area	

the National Institute of Neurological Diseases and Stroke.

1969 The Division of Environmental Health Sciences was renamed the National Institute of Environmental Health Sciences (NIEHS). The National Heart Institute was renamed the National Heart and Lung Institute.

1972 The National Institute of Arthritis and Metabolic Diseases was renamed the National Institute of Arthritis, Metabolism, and Digestive Diseases.

1974 The National Institute on Aging (NIA) was created.

1975 The National Institute of Neurological Diseases and Stroke was renamed the National Institute of Neurological and Communicative Disorders and Stroke (NINDS).

1976 The National Heart and Lung Institute was renamed the National Heart, Lung, and Blood Institute (NHLBI).

1981 The National Institute of Arthritis, Metabolism, and Digestive Diseases was renamed the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK).

1986 The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases was renamed the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) was created. The Center for Nursing Research was transferred from the Health Resources and Services Administration (HRSA) and renamed the National Center for Nursing Research.

1989 The National Institute on Deafness and Other Communication Disorders (NIDCD) was established. The National Institute of Neurological and Communicative Disorders and Stroke was renamed the National Institute of Neurological Disorders and Stroke (NINDS). The National Center for Human Genome Research was established. The National Center for Biotechnology Information was established within the NLM.

1990 The National Center for Research Resources (NCRR) was created by consolidating the Division of Research Services and the Division of Research Resources.

1992 The National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Drug Abuse (NIDA), and National Institute of Mental Health (NIMH) were transferred to the NIH from the Alcohol, Drug Abuse, and Mental Health Administration.

1993 The National Center for Nursing Research was renamed the National Institute of Nursing Research (NINR).

1995 The NIH was established as an HHS Operating Division, thereby elevating it to report directly to the Secretary of HHS.

1997 The National Center for Human Genome Research was renamed the National Human Genome Research Institute (NHGRI).

1998 The Division of Research Grants was renamed the Center for Scientific Review. The National Center for Complementary and Alternative Medicine (NCCAM) was established. The National Institute of Dental Research was renamed the National Institute of Dental and Craniofacial Research (NIDCR).

2001 The National Center on Minority Health and Health Disparities was established. The National Institute of Biomedical Imaging and Bioengineering (NIBIB) was established.

THE NATIONAL CANCER INSTITUTE

NCI Mission

The National Cancer Institute (NCI) is a component of the National Institutes of Health (NIH), one of 11 operating divisions that compose the Public Health Service (PHS) in the Department of Health and Human Services (HHS). The NCI, established under the National Cancer Act of 1937, is the Federal Government's principal agency for cancer research and training. The National Cancer Act of 1971 broadened the scope and responsibilities of the NCI and created the National Cancer Program. Over the years, legislative amendments have maintained the NCI authorities and responsibilities and added new information dissemination mandates as well as a requirement to assess the incorporation of state-of-the-art cancer treatments into clinical practice.

The National Cancer Institute is committed to dramatically lessening the impact of cancer. The NCI is the primary means of support for America's cancer research enterprise, whether in its own laboratories or in our Nation's research universities. The NCI is dedicated to the understanding, diagnosis, treatment, and prevention of cancer for all people. The NCI works toward this goal by providing vision to the Nation and leadership for both domestic and international NCI-funded researchers. The NCI also works to ensure that research results are applied in clinical practice and public heath related programs to reduce the burden of cancer for all populations.

Within this framework, NCI researchers work to more fully integrate discovery activities through interdisciplinary collaborations; accelerate development of interventions and new technology through translational research; and ensure the delivery of these interventions for application in the clinic and public health programs as state-of-the-art care for all those in need.

NCI and the National Cancer Program

As the leader of the National Cancer Program (NCP), the NCI provides vision and leadership to the global cancer community. The NCI conducts and supports research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer, rehabilitation, and the continuing care of cancer patients. Critical to the success of its programs are collaborations and partnerships that further NCI's progress in serving cancer patients and those who care for them.

The NCI supports a broad range of research to expand *scientific discovery* at the molecular and cellular level, within a cell's microenvironment, and in relation to human and environmental factors that influence cancer development and progression. Each year, almost 5,000 principal investigators lead research projects that result in better ways to combat cancer. Intramural research serves as a hub for new development through cutting-edge basic, clinical, and epidemiological research. Extramural program experts provide guidance and oversight for research conducted at universities, teaching hospitals, and other organizations. Proposals are selected for funding by peer review, a rigorous process by which scientific experts evaluate new proposals and recommend the most scientifically meritorious for funding. In addition to direct research funding, the NCI offers the Nation's cancer scientists a variety of useful research tools and services: tissue samples, statistics on cancer incidence and mortality, bioinformatic tools for analyzing data, databases of genetic information, and resources through NCI-supported Cancer Centers, Centers of Research Excellence, and the Mouse Models of Human Cancer Consortium.

The NCI also uses collaborative platforms and an interdisciplinary environment to promote *translational research and intervention development*. Discovery of a new tool that first helps to understand the underlying mechanism of cancer may eventually be used to help diagnose it, and then may be further developed to help treat it. For example, recent advances in bioinformatics and the related explosion of technology for genomics and proteomics research are dramatically accelerating the rate for processing large amounts of information for cancer screening and diagnosis. The largest collaborative research activity is the Clinical Trials Program for testing interventions for preventing cancer, diagnostic tools, and cancer treatments as well as providing access as early as possible to all who can benefit. The NCI supports over 1,300 clinical trials a year, assisting more than 200,000 patients.

The NCI research impacts the *delivery of improved cancer interventions to cancer patients and those who care for them*. Timely communication of NCI scientific findings help people make better health choices and advise physicians about treatment options that are more targeted and less invasive, resulting in fewer adverse side effects. NCI researchers also seek the causes

of disparities among underserved groups and gaps in quality cancer care, helping to translate research results into better health for groups at high risk for cancer, including cancer survivors and the aging population. In addition, the NCI fosters partnerships with other agencies and organizations to accelerate the pace for moving targeted drugs through the pipeline of discovery, development, and delivery.

Information about NCI's research and activities is available through its public Web site, http://cancer.gov.

NCI Legislative Authority

The NCI, established under the National Cancer Act of 1937, is the Federal Government's principal agency for cancer research and training. The National Cancer Act of 1971 broadened the scope and responsibilities of the NCI and created the National Cancer Program. Under the National Cancer Act of 1971, the Director of the NCI is authorized to submit, directly to the President, a professional judgment budget reflecting the full funding needs of the National Cancer Program. This budget is referred to as the Bypass Budget.

Bypass Budget

The mandate to produce a "Bypass Budget" is a special authority given to the NCI Director. The Bypass Budget builds on research successes and ensures that research discoveries are applied to improve human health, and allows the NCI Director to express to the President the plans and priorities of the NCI and the National Cancer Program, along with an indication of the associated costs.

Each year, the NCI produces this document to reflect the professional judgment of the Nation's top cancer experts about the realities of cancer research and control, and how much money could be spent wisely in the conduct of the entire program.

The authority to produce the Bypass Budget has many benefits. The extensive strategic planning process that is used to develop the Bypass Budget builds on research successes, supporting the cancer research workforce with the technologies and resources it needs. In addition to being submitted to the President, this comprehensive research plan also is provided to Congress, and is used by the greater cancer research community, professional organizations, advisory groups, advocacy organizations, and public and private policymakers. As a result, the Bypass Budget and its development serve as a planning process for the entire National Cancer Program, outlining clearly the areas of highest priority.

In addition to informing the President, the Bypass Budget document also serves as the Institute's strategic plan and has become a powerful communication and priority setting tool used by constituents across the National Cancer Program. Updated each year, the plan provides a guide for building on research successes, supporting the cancer research workforce with the technologies and resources it needs, and ensuring that research discoveries are applied to improve human health. This strategic plan is based on the authority and the responsibilities entrusted to the Presidentially appointed NCI Director to coordinate the research activities of the NCI with the other parts/members of the National Cancer Program.

In so doing, the Director is aided by the National Cancer Advisory Board (NCAB), a group composed of scientists, medical personnel, and consumers from all sectors, public and private, of the cancer enterprise who possess the needed expertise and experience to help formulate a national agenda in cancer research. The NCAB meets with the President's Cancer Panel (PCP) members, who have *ex officio* seats on the Board, to facilitate transfer of PCP observations on the barriers to progress in the NCP and the development of possible solutions. Their deliberations are directly coordinated with other government agencies through the participation of *ex officio* federal members representing key agencies involved in executing the National Cancer Program. For example, discussions at the NCAB meetings with *ex officio* members representing Department of Defense and Veterans Affairs health care systems directly led to the availability of NCI clinical trials through their health care systems. Close coordination across agencies is critical in the formulation of a strategic plan that takes advantage of the capabilities of each agency and the constituencies it serves.

The ability of the NCI and its partners to address the initiatives in the Bypass Budget is a measure of the success of the NCP. In this way, the Bypass Budget enables efficient strategic coordination of the NCP.

As part of the evaluation process, the Presidentially appointed PCP is charged to review the implementation of such plans and identify directly for the President and the Nation the extent of their success.

NCI Organizational Structure

The NCI's current organizational structure can be seen in Exhibit V. NCI's Office of the Director serves as the focal point for the NCP, with advice from the President's Cancer Panel, the NCAB, the Board of Scientific Counselors (BSC), and the Board of Scientific Advisors (BSA). The BSA gives final concept approval for extramural Requests for Applications (RFAs) and Requests for Proposals (RFPs), while the BSC conducts intramural laboratory and branch reviews. The Director of the Institute is assisted by several Deputy Directors: Dr. Alan Rabson, Deputy Director, NCI; Dr. Douglas Lowy, Deputy Director, NCI; Dr. James Doroshow, Deputy Director, NCI; and Mr. John Czajkowski, Deputy Director for Management, NCI. The Scientific Program Leadership (SPL) Committee of the Institute (see Appendix A) includes the Director, Deputy Directors, Division Directors, and other senior scientific staff. The SPL meets on a regular basis to discuss various matters of NCI policy, including but not limited to review and approval of RFA and research and development contract concepts before review by the BSA; review of program announcements; development of funding plans; grant payment by exceptions, etc. NCI's cancer research activities are monitored and administrated through several extramural and intramural divisions, centers, and offices.

Office of the Director

Examples of offices and centers within the Office of the Director include:

NCI Center for Biomedical Informatics and Information Technology (CBIIT)
The NCI Center for Bioinformatics (NCICB) helps speed scientific discovery and facilitates translational research by building many types of tools and resources that enable information to be shared along the continuum from the scientific bench to the clinical bedside and back. The NCICB (1) coordinates and deploys informatics in support of NCI research initiatives; (2) provides all manner of informatics support, including platforms, services, tools, and data to NCI-supported research initiatives; (3) participates in the evaluation and prioritization of NCI's bioinformatics research portfolio; (4) conducts or facilitates research that is required to fulfill NCI's bioinformatics requirements; (5) serves as the focus for strategic planning to address NCI's expanding research initiative's informatics needs; (6) establishes bioinformatics technology standards (both within and outside of the NCI); (7) communicates, coordinates, and establishes bioinformatics exchange standards; and (8) provides direct support to several NCI research programs, such as: the Cancer Genome Anatomy Project (CGAP), the Mouse Models of Human Cancer Consortium (MMHCC), the Director's Challenge: Towards a Molecular Classification of Cancer, and Clinical Trials. It also develops core infrastructure to support the integration of these efforts.

Office of Communications and Education (OCE)
The OCE advances the mission of NCI by disseminating research results to the public to improve the lives of those affected by cancer. Working closely with scientists and partners, OCE uses effective methods to reach diverse audiences and meet their needs for the latest, evidence-based cancer information.

Center to Reduce Cancer Health Disparities (CRCHD)
The CRCHD is the keystone of NCI's efforts to reduce the unequal burden of cancer in our society. As the organizational focus for these efforts, the Center directs and supports initiatives that advance the understanding of what causes health disparities. It also supports programs that develop and integrate effective interventions to reduce or eliminate these disparities. The CRCHD, through its Diversity Training Branch (DTB), leads NCI's efforts in the training of students and investigators from diverse populations who will be part of the next generation of competitive researchers in cancer and cancer health disparities research.

Office of Advocacy Relations (OAR)
The OAR engages the advocacy and NCI communities in dialogue about cancer research opportunities and priorities to advance progress and improve outcomes. The OAR (1) serves as the Institute's expert and central resource for advocacy matters; (2) facilitates dynamic relationships and collaborations to promote mutual goals; and (3) disseminates information and fosters understanding of key cancer issues and priorities.

Center for Strategic Scientific Initiatives
The Center for Strategic Scientific Initiatives (CSSI) directs the planning, development, and implementation of a number of strategic scientific and technology initiatives and partnerships that emphasize innovation, transdisciplinary teams, and convergence of scientific disciplines to enable progress against cancer. These programs also stress the development and application of advanced technologies, the synergy of large-scale and individual initiated research, novel partnerships, and translation of discoveries into new interventions to detect, prevent, and treat cancer more effectively.

Exhibit V. The National Cancer Institute

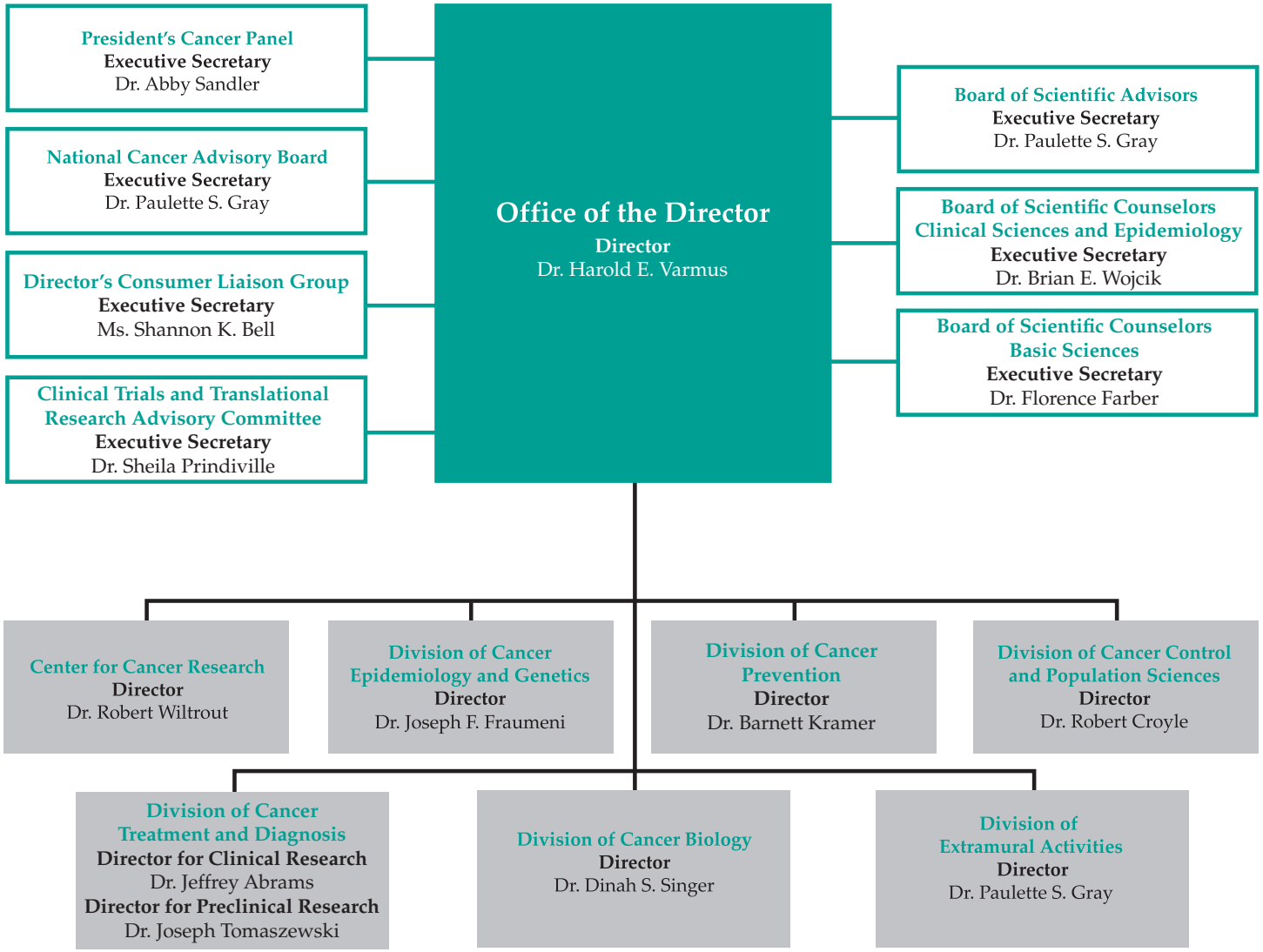
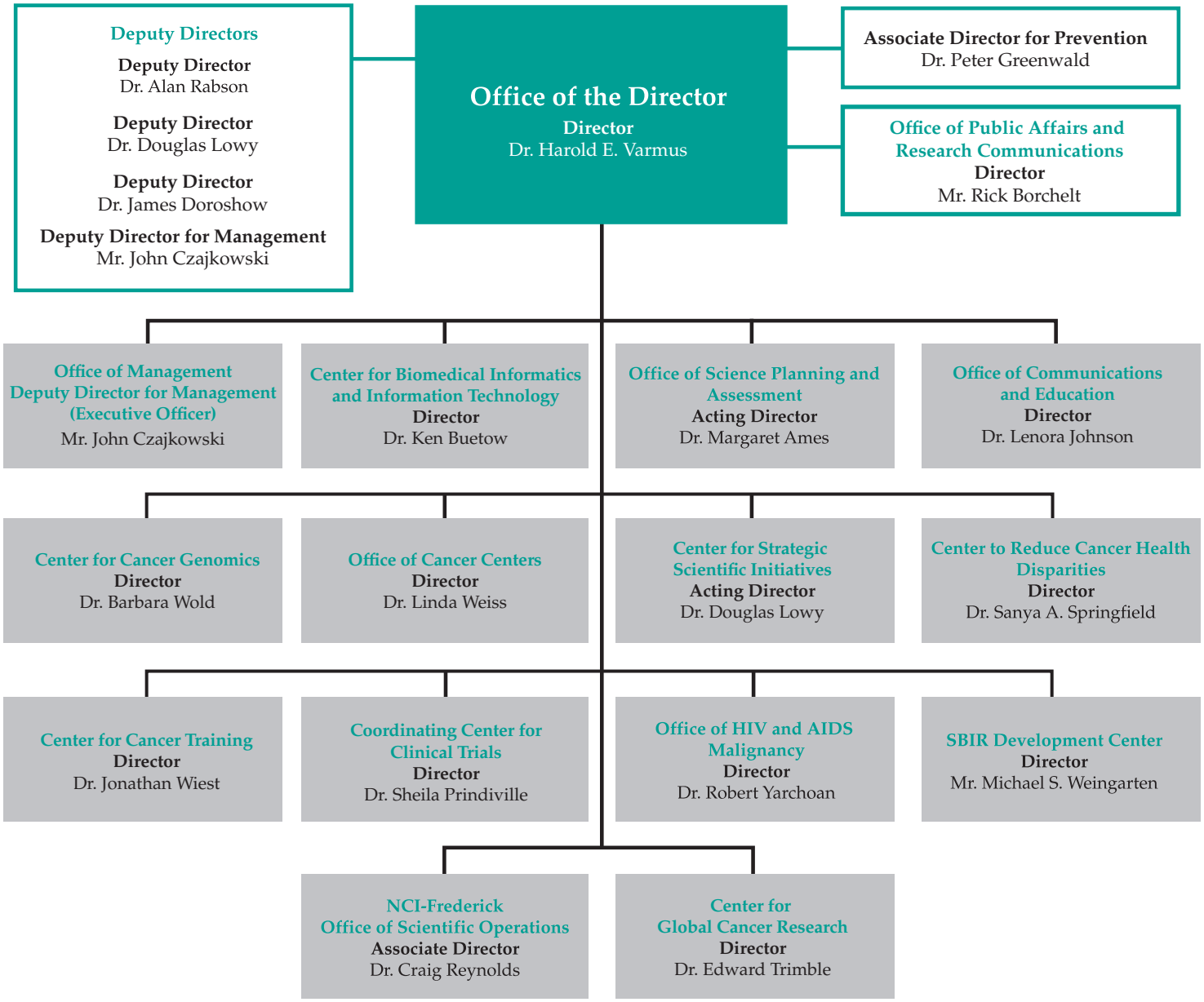


Exhibit V. The National Cancer Institute (Continued)



Several offices in CSSI are committed to accelerating the progress of cancer research through its technology-driven initiatives, collaboration with other government programs, and engagement with the private sector in the areas of nanotechnology, proteomics, cancer genomics, and biospecimen resources. By placing a heavy emphasis on advanced technology development, the NCI is accelerating the creation and use of tools that are already facilitating the translation of basic knowledge into clinical advances to benefit patients with a new generation of molecularly based diagnostics and therapeutics. Programs include: Alliance for Nanotechnology in Cancer, Clinical Proteomic Technologies Initiative, Innovative Molecular Analysis Technologies, and Physical Sciences in Oncology.

Office of Cancer Centers
Currently, the Office supports 66 NCI-designated cancer centers nationwide that are actively engaged in transdisciplinary research to reduce cancer incidence, morbidity, and mortality. The NCI-designated Cancer Centers (P30) are a major source of discovery of the nature of cancer and of the development of more effective approaches to cancer prevention, diagnosis, and therapy. Comprehensive Cancer Centers also deliver medical advances to patients and their families, educate health-care professionals and the public, and reach out to underserved populations. Cancer Centers are characterized by strong organizational capabilities, institutional commitment; and transdisciplinary, cancer-focused science; experienced scientific and administrative leadership; and, state-of-the-art cancer research and patient care facilities.

Center for Cancer Training (CCT)
The CCT is responsible for: (1) coordinating and providing research training and career development activities for fellows and trainees in NCI's laboratories, clinics, and other research groups; (2) developing, coordinating, and implementing opportunities in support of cancer research training, career development, and education at institutions nationwide; and (3) identifying workforce needs in cancer research and adapting NCI's training and career development programs and funding opportunities to address these needs.

Coordinating Center for Clinical Trials (CCCT)
The CCCT is central to NCI's efforts to accelerate the delivery of new tools into the clinic through its translational science and clinical trial enterprises. The CCCT facilitates collaborations that expedite translational and clinical cancer research by:

- Supporting the implementation of the Clinical Trials Working Group and Translational Research Working Group recommendations;
- Facilitating prioritization of the NCI's most important clinical trials by Scientific Steering Committees working with NCI clinical programs;
- Partnering with the NCI's Center for Biomedical Informatics and Information Technology (CBIIT) to establish the Clinical Trials Reporting Program (CTRP), a comprehensive database with current information on all NCI-funded clinical trials.

Center for Cancer Genomics (CCG)
The CCG is focused on understanding the molecular mechanisms of cancer, with the ultimate goal of improving the prevention, early detection, diagnosis, and treatment of cancer. To meet this goal, the CCG:

- Provides information, technology, methods, informatics tools, and reagents to serve the needs of the cancer research community.
- Manages the following research programs: the Cancer Genome Anatomy Project (CGAP), the NIH Mammalian Gene Collection (MGC), the Initiative for Chemical Genetics (ICG), the Cancer Genome Atlas (TCGA), the Cancer Genetic Markers of Susceptibility (CGEMS), and Therapeutically Applicable Research to Generate Effective Treatments (TARGET).

Office of Biorepositories and Biospecimen Research (OBBR)
The OBBR is responsible for coordinating and developing the Institute's biospecimen resources and capabilities and ensuring that human biospecimens available for cancer research are of the highest quality. This is being accomplished through the development of a common biorepository infrastructure that promotes resource sharing and team science to facilitate multi-institutional, high throughput genomic and proteomic studies.

Center for Global Cancer Research (CGCR)
The CGCR coordinates NCI's worldwide activities in a number of arenas, including: liaison with foreign and international agencies and other U.S. government agencies involved in global health; coordination of cancer research activities under agreements between the United States and other countries; planning and implementation of international scientist exchange programs; sponsorship

of international workshops; and dissemination of cancer information.

Office of Science Planning and Assessment (OSPA)
OSPA's primary responsibilities are to develop and coordinate NCI's scientific planning and evaluation activities. OSPA staff accomplish this through consultation, guidance, analysis, and document preparation in support of various Institute-wide and division-level programs. These critical activities enable the NCI to identify needs and opportunities for cancer research, establish research goals, and develop sound plans for reaching those goals.

Office of HIV and AIDS Malignancy (OHAM)
The Office of HIV and AIDS Malignancy (1) coordinates and works with the Divisions and other Offices to manage the portfolio of HIV/AIDS and AIDS malignancy research within the NCI; (2) advises the NCI Director and other NCI managers on issues related to research in HIV/AIDS and AIDS malignancies; (3) coordinates, helps prioritize, and facilitates the NCI research effort in HIV/AIDS and AIDS malignancies and works with NCI management to redirect the HIV/AIDS and AIDS malignancy research effort, as appropriate, into the highest priority areas; (4) interfaces with the NIH Office of AIDS Research (OAR) and other ICs regarding research in HIV/AIDS and AIDS malignancies in the NCI; and (5) directly manages certain AIDS and AIDS malignancy research programs, such as the AIDS and Cancer Specimen Resource, the AIDS-Associated Malignancies Clinical Trial Consortium (AMC), the NCI Component of the Centers for AIDS Research (CFARS), and the NCI component of the Women's Interagency HIV Study (WIHS).

Small Business Innovation Research (SBIR) Development Center
The SBIR Development Center serves as the NCI focal point for the management of all Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Program activities, and implementation of pertinent legislation, rules and regulations and associated matters related to the SBIR/STTR Program consisting of grant and contractor awards and providing expertise, advice, and services to applicants and NCI programs.

NCI-Frederick Office of Scientific Operations
The NCI-Frederick Office of Scientific Operations (1) oversees and manages scientific operations at NCI-Frederick and serves as the Project Office for the three main operation and support contracts at NCI-Frederick; (2) directs and develops advanced technologies that are made available to customers of NCI-Frederick; (3) implements programmatic decisions approved by the NCI Director and the Associate Director for NCI-Frederick to transition new efforts to NCI-Frederick by developing contractual requirements and budgets, arranging for needed space, and providing technical and project management advice to the Contracting Officer; (4) works closely with customers (including other NCI and NIH components, the Food and Drug Administration, the Department of Defense, the Department of Agriculture, and the Department of Homeland Security) and contractors to ensure that contractors understand customers' needs and that the customers receive planned outcomes; (5) assists the NCI Associate Director for Frederick with the administrative and business operations of NCI-Frederick; (6) assists the NCI Associate Director for Frederick with planning and prioritizing of space and the maintenance of all buildings and grounds; (7) monitors contractor performance, obtains customer satisfaction feedback, and provides this information to the Management Operations and Support Branch for the Award Fee processes; (8) tracks and reports funds received and costs associated with all work performed at NCI-Frederick; (9) develops and manages educational, employee outreach, and public outreach programs, including programs for K-12 students and internship opportunities for high school and undergraduate students; (10) coordinates the expansion of student/fellowship mentoring programs at NCI-Frederick; and (11) coordinates NCI-Frederick facility "activities" such as the Spring Research Festival; Take Your Child to Work Day; the Summer Student Seminar Series; Summer Student Poster Day; the Housing Resources List; speaker requests; and visits for students, teachers, and other interested groups.

Extramural Divisions

The extramural research and research-related activities of the NCI are conducted by five divisions under the supervision of the Office of the Director. The functions of the divisions and the major areas of research and research support activities for which each is responsible are:

Division of Cancer Biology (DCB)
The mission of the DCB is to ensure continuity and stability in basic cancer research, while encouraging and facilitating the emergence of new ideas, concepts, technologies, and possibilities. The DCB strives to achieve this goal by promoting a balance between the continued support of existing

research areas and selective support of emerging research areas. The DCB provides guidance, advice, funding information, and financial support to grantees and applicants. The DCB encourages the expansion of new research areas through a range of initiatives and funding mechanisms. The scientific discoveries from this research base are critical to the goal of the NCI since they form the intellectual and scientific foundation on which strategies for the prevention, diagnosis, and treatment of cancer are developed. (http://dcb.nci.nih.gov/)

Division of Cancer Control and Population Sciences (DCCPS)
The DCCPS aims to reduce the risk, incidence, and number of deaths from cancer, as well as to enhance the quality of life for cancer survivors. This division conducts and supports an integrated program of the highest quality genetic, epidemiologic, behavioral, social, applied, and surveillance cancer research. DCCPS funded research aims to: (1) understand the causes and distribution of cancer in various populations, (2) support the development and implementation of effective interventions, and (3) monitor and explain cancer trends in all segments of the population. Central to these activities is a process of synthesis and decision making, which aids in evaluating what has been learned, identifying new priorities and strategies, and effectively applying research discoveries to reduce the cancer burden at the population level. (http://dccps.nci.nih.gov)

Division of Cancer Treatment and Diagnosis (DCTD)
The DCTD attempts to identify and exploit the most promising areas of science and technology and to initiate, enable, and conduct research that will yield important new knowledge that is likely to lead to better diagnostic or therapeutic interventions in the various childhood and adult cancers. The division administers grants, contracts, and cooperative agreements, and offers strategically planned workshops and conferences with scientists, clinicians, and public and private partners. It also sponsors a vigorous program of in-house applied research linked to investigators and goals in the extramural community. (http://dctd.cancer.gov/)

Division of Cancer Prevention (DCP)
The DCP plans and conducts programs in basic and applied research and development, technology transfer, demonstration, education, and information dissemination. DCP's programs are designed to: expedite the use of new information relevant to the prevention, detection, and diagnosis of cancer; expedite the use of new information about pretreatment evaluation, treatment, rehabilitation, and continuing care; plan, direct, and coordinate the support of research on cancer prevention at Cancer Centers and community hospitals, and through organ systems programs; support cancer research training, clinical education, continuing education, and career development in cancer prevention; coordinate program activities with other divisions, Institutes, and Federal and state agencies; and establish liaison with professional and voluntary health agencies, Cancer Centers, labor organizations, cancer organizations, and trade associations. (http://www.prevention.cancer.gov/)

Division of Extramural Activities (DEA)
The mission and responsibilities of the DEA in some way affect all extramural scientists receiving research or training support from the NCI. The DEA coordinates the review of special initiatives, large grants, and contracts. It is involved in all aspects of grant development and tracking, from the original conception of extramural research and training programs to follow-up after funds are dispersed. In brief, the DEA was established to: provide advice and guidance to potential applicants; receive and refer incoming grant applications to appropriate programs within the NCI; provide the highest quality and most effective scientific peer review and oversight of extramural research; coordinate and administer Federal advisory committee activities related to the various aspects of the NCI mission, such as the NCAB and BSA; establish and disseminate extramural policies and procedures, such as requirements for inclusion of certain populations in research, actions for ensuring research integrity, or budgetary limitations for grant applications; and track the NCI research portfolio (more than 7,500 research and training awards) using consistent, budget-linked scientific information to: (1) provide a basis for budget projections and (2) serve as a resource for the dissemination of information about cancer. (http://deainfo.nci.nih.gov/funding.htm)

Intramural Center and Division

Center for Cancer Research (CCR)
As the intramural component of the NCI, the CCR conducts basic clinical investigations at the Bethesda campus. The mission of the CCR is to reduce the burden of cancer through exploration, discovery, and translation. It provides a new forum for cancer research without scientific, institutional, or administrative barriers. The Center is achieving this by conducting outstanding, cutting-edge, basic

and clinical research on cancer and translating these discoveries into treatment and prevention. The overall goal is to form a highly interactive, interdisciplinary group of researchers who have access to technology and are able to participate in clinical investigations. The CCR also maintains a foundation of investigator-initiated, independent research. CCR scientists conduct innovative basic and clinical research aimed at discovering the causes and mechanisms of cancer to improve the diagnosis, treatment, and prevention of cancer and other diseases. (http://ccr.nci.nih.gov/)

Division of Cancer Epidemiology and Genetics (DCEG)
The DCEG is an intramural research program in which scientists conduct an international program of population-based studies to identify environmental and genetic determinants of cancer. In carrying out its mission, the DCEG is at the cutting edge of approaches to untangle complex gene-environment and gene-gene interactions in cancer etiology. To conduct these studies, investigators at all levels of their careers work collaboratively to bring together a variety of scientific disciplines. (http://dceg.cancer.gov/)

NCI Advisory Committees

President's Cancer Panel (PCP)
The President's Cancer Panel (see Appendix C) is an NCI Federal advisory committee that reports directly to the U.S. President on the activities of the National Cancer Program. The panel was established by the Public Health Service Act, as amended by the National Cancer Act (P.L. 92-218), and was chartered in accordance with the Federal Advisory Committee Act (P.L. 92-463). The Panel consists of three members who are appointed by the President for terms of 3 years. One of the members is appointed by the President as Chairperson of the Panel for a 1-year term. At least two members must be distinguished scientists or physicians, and the third may be a lay person. The panel, which meets at least four times a year, is responsible for monitoring the development and execution of the National Cancer Program, evaluating its efficacy, making suggestions for its improvement, and submitting periodic progress reports to the President.

National Cancer Advisory Board (NCAB)
The NCAB (see Appendix D) advises, assists, consults with, and makes recommendations to the Secretary of the HHS, and the Director of NCI, regarding the activities carried out by and through the Institute as well as policies regarding these activities. The NCAB may make recommendations regarding support grants and cooperative agreements, technical and scientific peer review, and functions pertaining to the NCI as described under sections 405, 406, 413, and 414 of the PHS Act, as amended.

The NCAB may implement procedures for expediting *en bloc* concurrence of Scientific Review Group recommendations. Several members may be selected by the Chair and/or Executive Secretary to provide *en bloc* concurrence on behalf of the Board. Only those applications that do not require individual consideration are included in this expedited process. A report of the *en bloc* recommendations is presented at each Board meeting.

Board of Scientific Advisors (BSA)
The BSA (see Appendix E) advises NCI's Director and Deputy Directors, and the Director of each NCI division, on a wide variety of matters. Topics include scientific program policy and the progress and future direction of each division's extramural research programs. The BSA's responsibilities include the evaluation of NCI awarded grants, cooperative agreements, and contracts, as well as concept review of those activities that it considers to be meritorious and consistent with the Institute's programs. The advisory role of the Board is scientific and does not include deliberation on matters of public policy. As necessary, the Board and its subcommittees may call upon special consultants, assemble *ad hoc* working groups, and convene conferences, workshops, or other activities.

Board of Scientific Counselors (BSC)
The BSC (see Appendixes F and G) advises the Directors of NCI's Intramural Division of Cancer Epidemiology and Genetics (DCEG) and Center for Cancer Research (CCR) and the Director and Deputy Directors of the NCI, on a wide variety of matters concerning scientific program policy and the progress and future direction of each of the intramural research programs. The BSC evaluates performance and productivity of each division, including the staff scientists, through periodic site visits to intramural laboratories. It also offers advice on the course of programs composing DCEG and CCR.

Director's Consumer Liaison Group (DCLG)
The DCLG (see Appendix H) provides advice to the Director, National Cancer Institute (NCI), with respect to promoting research outcomes that are in the best interest of cancer patients. To this end, the DCLG will conduct these activities with

the intent to identify new approaches, promote innovation, recognize unforeseen risks or barriers, and identify unintended consequences that could result from NCI decisions or actions. Additionally, the DCLG will provide insight into enhancing input, optimizing outreach, and promoting strong collaborations, all with respect to non-scientist stakeholders.

Clinical Trials and Translational Research Advisory Committee (CTAC)
The Committee (see Appendix I) advises, assists, consults with, and makes recommendations to the Director, NCI, NCI Deputy Directors, and the Director of each NCI Division on the NCI-supported national clinical trials enterprise to build a strong scientific infrastructure by bringing together a broadly developed and engaged coalition of stakeholders involved in the clinical trials process. This encompasses oversight of all trials both extramural and intramural. The Committee will provide broad scientific and programmatic advice on the investment of tax payer dollars in clinical trials and supportive science. In addition, the Committee makes recommendations regarding the effectiveness of NCI's translational research management and administration program, including needs and opportunities across disease sites, patient populations, translational developmental pathways, and the range of molecular mechanisms responsible for cancer development. The Committee will advise on the appropriate magnitude for dedicated translational research priorities and recommend allocation of translational research operations across organizational units, programs, disease sites, populations, developmental pathways, and molecular mechanisms. The Committee will ensure that appropriate emphasis is placed on rare cancers, medically underserved populations, and historically lower resourced pathways to clinical goals. The goal is to foster an open, collaborative system involving all the critical stakeholders in the prioritization process bringing diverse institutions and individuals together into an integrated and efficient, but innovative and responsive effort, thus moving therapies to patients.

Initial Review Group (IRG)
The IRG advises the Director of the NCI, and the Director, Division of Extramural Activities, NCI, on the scientific and technical merit of applications for grants for research, research training, research-related grants and cooperative agreements, or contract proposals relating to scientific areas relevant to carcinogenesis, cancer biology and diagnosis, Cancer Center administration, medicine, radiological and surgical oncology, cancer chemotherapy, cancer epidemiology, cancer prevention and control, cancer education, cancer information services, community outreach, cancer detection and diagnosis, cancer treatment and restorative care, dentistry, nursing, public health, nutrition, education of health professionals, medical oncology, surgery, radiotherapy, gynecologic oncology, pediatric oncology, pathology, and biostatistics. The IRG is composed of several chartered subcommittees that primarily review the following applications: Cancer Centers, institutional training grants, and career development awards.

NCI Programs and Activities

Research Programs

The Institute conducts and leads intensive work to advance knowledge of cancer's biology and processes; to discover and develop new interventions; and to employ a bench-to-bedside approach that strives to rapidly make new treatments—our latest science—available to patients in the communities where they live. Across these complex endeavors, the NCI works to foster the collaborations of government, the private sector, and academia. In addition to the broad range of both basic and applied laboratory and clinical programs that it supports, the NCI provides various research support services, including the development and distribution of critical materials such as viruses, animals, equipment, tissues, and standardized reference bibliographies. These activities are conducted within the divisions and centers of the NCI, under the supervision of the Office of the Director.

Cancer Causation
Cancer causation research concentrates on the events involved in the initiation and promotion of cancer. It encompasses chemical and physical carcinogenesis, biological carcinogenesis, epidemiology, chemoprevention, and nutrition research. Studies in this area focus on external agents such as chemicals, radiation, fibers, and other particles, as well as viruses, parasitic infections, and host factors such as hormone levels, nutritional and immunologic status, and the genetic endowment of the individual. FY2010 cancer causation research expenditures totaled about $1.18 billion, accounting for 23.3 percent of the total NCI budget.

Detection and Diagnosis
Detection and diagnosis research includes studies designed to improve diagnostic accuracy; provide better prognostic information to guide therapeutic decisions; monitor the response to therapy more

effectively; detect cancer at its earliest presentation; and identify populations and individuals at increased risk for the development of cancer.

Areas of emphasis include: improvements in the detection and diagnosis of breast, cervical, uterine, and prostate cancer; the transfer of molecular technologies from the laboratory to clinical practice; the identification of better prognostic markers; increased availability of human tumor samples with associated clinical information; and research to identify genetic alterations involved in tumor pathogenesis and behavior. FY2010 detection and diagnosis research expenditures totaled about $429 million, accounting for 8.4 percent of the total NCI budget.

Treatment
Treatment research is composed of preclinical and clinical research. Preclinical research focuses on the discovery of new antitumor agents and their development in preparation for testing in clinical trials. These agents include both synthetic compounds and natural products. Clinical research (see Appendix J) involves demonstrating the effectiveness of new anticancer treatments through systematic testing in clinical trials. Phase I trials establish the maximum tolerated dose of a new agent; Phase II trials examine its efficacy against a variety of cancers; and Phase III trials compare the new treatment with the best standard therapy, in terms of improved survival and decreased toxicity. FY2010 treatment research expenditures totaled about $1.16 billion, accounting for 22.7 percent of the total NCI budget.

Cancer Biology
Cancer biology supports a broad spectrum of basic research on cancer and the body's response to cancer. Studies include investigations of cellular and molecular characteristics of tumor cells, interactions among cells within a tumor, and the components of the host immune defense mechanisms. Cancer is the result of genetic damage that accumulates in stages. It is the goal of cancer biology to identify and explain the stepwise progression between the initiating event in the cell and final tumor development. FY2010 cancer biology expenditures totaled approximately $783 million, accounting for 15.4 percent of the total NCI budget.

Cancer Prevention and Control
The NCI conducts Cancer Prevention and Control basic and applied research through both intramural and extramural mechanisms in all phases of cancer prevention and control, as well as cancer surveillance. A key priority of this program is to develop strategies for the effective translation of knowledge gained from prevention and control research into health promotion and disease prevention activities for the benefit of the public. An integrated system of basic research, clinical trials, and applications research is in place and seeks to promote cancer prevention and control activities across the country.

The Cancer Prevention and Control Program includes four components and several subprograms, many of which relate to other program activities of the NCI, including information dissemination, epidemiology, and cancer treatment. The four components are Cancer Prevention Research, Cancer Control Science, Early Detection and Community Oncology, and Cancer Surveillance. FY2010 Cancer Prevention and Control Program expenditures totaled approximately $364 million, accounting for 7.1 percent of the total NCI budget.

Resource Development

Cancer Centers
The Cancer Centers Program consists of a group of nationally recognized, geographically dispersed, individual institutions with outstanding scientific reputations. Each institution reflects particular research talents and special technological capabilities. In FY2010, there were 66 centers, which received a total of $295.8 million in support, accounting for 5.81 percent of the total NCI budget.

The NCI uses the Cancer Center Support Grant (CCSG) mechanism (P30) to support centers that conduct research and outreach activities on several different cancers. Cancer Centers are designated as either cancer centers or comprehensive cancer centers.

Cancer Centers have developed in a number of different organizational settings. Some are independent institutional entities entirely dedicated to cancer research (free-standing centers); some have been formed as clearly identifiable entities within academic institutions and promote interactive cancer research programs across departmental and/or college structures (matrix centers); and others involve multiple institutions (consortium centers).

The CCSG is intended to provide support to the peer-reviewed research base of the Cancer Center within the larger institution. The CCSG supports the operational framework (infrastructure) of the center and partially pays for shared laboratory resources and facilities. Research projects themselves are supported through the individual grants and contracts from the NIH and from a variety of other grant funding agencies and organizations.

Specialized Programs of Research Excellence
The Specialized Programs of Research Excellence (SPOREs) are designed to stimulate translational research from the laboratory to clinical practice. SPOREs, which are funded under the P50 grant mechanism, focus on research in prevention, detection, diagnosis, and treatment for a single cancer site. These are awarded to institutions that demonstrate the ability to perform significant translational research.

Comprehensive Minority Institution/Cancer Center Partnership
NCI's Comprehensive Minority Institution/Cancer Center Partnership (U54) awards are cooperative agreements designed to establish comprehensive partnerships between the Minority Serving Institution (MSI) and the NCI-designated Cancer Centers. The partnership focuses on cancer research and one or more target areas in cancer research, training and career development, education, or outreach activities designed to benefit racial and/or ethnic minority populations in the region the Cancer Center serves. The partnership also creates a stable, long-term, collaborative relationship between the MSI and NCI-designated Cancer Centers and raises awareness about problems and issues relevant to the disproportionate rates of cancer incidence and mortality in minority populations.

Research Manpower Development
The Cancer Training Branch (CTB) in the Center for Cancer Training manages the Institute's extramural research training, career development, and education programs, and provides guidance to the extramural biomedical research community and administration of awards. This assures continued development of well-trained investigators in the basic, clinical, population, and behavioral sciences, who are prepared to address problems in cancer biology, causation, prevention and control, detection and diagnosis, treatment, and rehabilitation. Operationally, the CTB has three functions. The first is the management of NCI-funded grants in research training, career development, and cancer education. The second function is the administration of the Ruth L. Kirschstein National Research Service Award (NRSA) components (F32 and T32) of the CTB grant portfolio. The NRSA program is the major mechanism for providing long-term, stable support to a wide range of promising scientists and clinicians. Individual awards are made directly to postdoctoral fellows (F32), and institutional awards (T32) are made to scientists who, together with a group of faculty-preceptors, administer a comprehensive training program for pre- and postdoctoral trainees. CTB administers a research career development program that supports the training of both scientists and research physicians during the first 3 to 5 years between receipt of a Ph.D., M.D., or other professional degree and receipt of an individual, investigator-initiated award. Among the career mechanisms are three additional non-NRSA institutional mechanisms (K12, R25T, and R25E) and six individual career development awards (K-series). The third function is the oversight and coordination of the NIH Loan Repayment Program. Program expenditures in FY2010 totaled approximately $178 million, accounting for 3.4 percent of the total NCI budget.

NCI Funding Mechanisms

The NCI supports cancer research, cancer control, and cancer support activities through an extramural program of grants, cooperative agreements, and contracts, and through an intramural program of in-house research. In accordance with NIH tradition, the Institute's extramural programs emphasize grant-supported, investigator-initiated research projects, which are conducted at both nonprofit and for-profit institutions in the United States and abroad. Research contracts are awarded to both nonprofit and for-profit institutions. Intramural funds support continuing investigations by NCI research scientists. The cooperative agreement mechanism, which is a cross between a grant and a contract, became available in 1979 as an additional procurement mechanism. Annual appropriations from Congress provide the funds for all research supported by the NCI.

Exhibit VI illustrates the relationship between total NCI obligations and the grant, contract, and intramural/other components of the NCI budget from 2000 to 2010. Exhibit VII shows the 2006-2010 budgets for various disease research areas. Exhibit VIII summarizes the FY2010 budget obligations by mechanisms. Exhibit IX shows the RPG awards by activity code and presents the number of grants awarded, the total dollars awarded, and the average cost of a grant for the period 2001–2010.

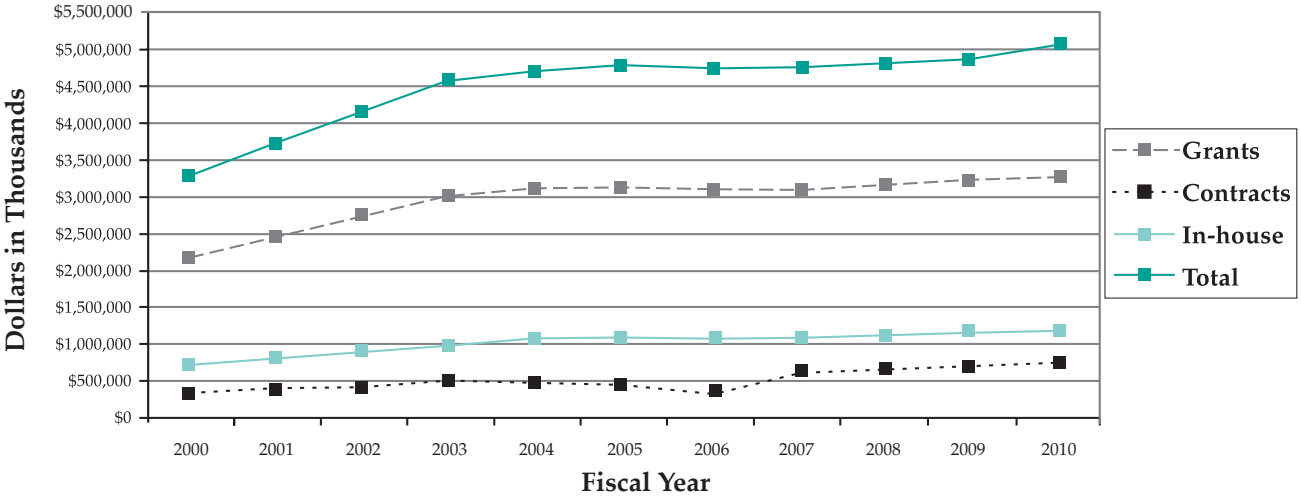
Grants

I. Research Project Grants

Research Project Grants are awards for investigator-initiated research applications. Several types of awards are made in this category; they vary in type of mechanism, type of applicant, total amount of support, and length of time. FY2010 research project grant expenditures totaled approximately $2.168 billion, accounting for 42.5 percent of the total NCI budget.

Exhibit VI. NCI Funding History*

	2000	2001	2002	2003	2004	2005	2006	2007	2007	2009	2010
Grants	$2,204,716	$2,488,627	$2,790,485	$3,047,650	$3,171,792	$3,251,216	$3,227,919	$3,174,713	$3,145,011	$3,182,832	$3,289,368
Contracts	361,355	411,588	437,610	532,760	514,602	504,798	492,822	558,510	586,883	618,062	621,682
In-house	745,010	853,50	948,606	1,011,936	1,037,499	1,038,730	1,026,484	1,059,392	1,095,658	1,166,033	1,187,097
Total	3,311,081	3,753,721	4,176,701	4,592,346	4,723,893	4,794,744	4,747,225	4,792,615	4,827,552	4,966,927	5,098,147



*Source: *NCI Fact Book*, FY2010.

P01 Research Program Project Grant
Research Program Project Grants (P01s) support an integrated, multiproject research approach involving a number of independent investigators who share knowledge and common resources. A P01 has a defined, central research focus involving several disciplines or several aspects of one discipline. Each individual project should contribute or be directly related to the common theme of the total research effort, thus forming a system of research activities and projects directed toward a well-defined research program goal.

R01 Research Project Grant
Research Project Grants (R01s) support a discrete, specified research project to be performed by the named investigator(s) in an area representing his/her specific interest and competencies. This is generally referred to as a "traditional research project grant."

R03 Small Research Grant
Small Research Grants (R03s) provide research support that is limited in time and amount, for studies in categorical program areas. Small research grants provide flexibility and are generally used to initiate studies for preliminary, short-term projects. These grants are nonrenewable.

R21 Exploratory/Developmental Grant
Exploratory/Developmental Grants (R21s) support the development of new research activities in categorical program areas. Support generally is restricted, in terms of the level of support and time.

R33 Exploratory/Developmental Grant—Phase II
Phase II Exploratory/Developmental Grants (R33s) provide additional support to innovative, exploratory, and developmental research activities that were initiated under the R21 mechanism.

R37 Method to Extend Research in Time (MERIT) Award
MERIT Awards (R37s) provide long-term grant support to investigators whose research competence and productivity are distinctly superior and who are highly likely to continue to perform in an outstanding manner. Investigators may not apply for a MERIT Award. After initial review, NCI staff and the NCAB review competing R01 applications to select MERIT awardees. An initial, 5-year MERIT Award is followed by possible extensions of 1 to 5 more years of support. Extensions are based upon an expedited review of the investigator's accomplishments during the initial period.

Exhibit VII. Research Funding for Various Research Areas (Dollars in Millions)*

Disease Area	2006 Actual	2007 Actual	2008 Actual	2009 Actual	2010 Actual
Total NCI Budget	**$4,747.2**	**$4,792.6**	**$4,827.6**	**$4,966.9**	**$5,098.1**
AIDS	253.7	253.7	258.5	265.9	272.1
Brain & CNS	130.3	148.2	153.7	151.5	156.8
Breast Cancer	584.7	572.4	572.6	599.5	631.2
Cervical Cancer	83.3	82.4	76.8	70.8	77.0
Clinical Trials	822.3	843.7	853.2	846.6	852.3
Colorectal Cancer	244.1	258.4	273.7	264.2	270.4
Head and Neck Cancers	71.3	66.2	76.1	76.8	62.7
Hodgkin's Disease	20.9	16.5	17.5	18.2	14.6
Leukemia	223.5	205.5	216.4	220.6	239.7
Liver Cancer	62.7	67.7	74.2	70.3	72.6
Lung Cancer	242.9	226.9	247.6	246.9	281.9
Melanoma	08.0	97.7	110.8	103.7	102.3
Multiple Myeloma	30.3	32.3	41.5	45.2	48.5
Non-Hodgkin's Lymphoma	114.1	113.0	122.6	130.9	122.4
Ovarian Cancer	95.1	96.9	100.0	110.1	112.3
Pancreatic Cancer	74.2	73.3	87.3	89.7	97.1
Prostate Cancer	293.2	296.1	285.4	293.9	300.5
Stomach Cancer	11.5	12.0	12.4	15.4	14.5
Uterine Cancer	19.4	16.6	17.1	18.0	14.2

*Source: *NCI Fact Book,* FY2010.

R41 Small Business Technology Transfer (STTR) Grant—Phase I
Phase I STTR Grants (R41s) support cooperative research and development projects between research institutions and small, domestic, for-profit organizations. R41s are limited in time and amount and are used to establish the technical merit and feasibility of ideas that have a potential for commercialization. Generally, support for Phase I STTR awards may not exceed $100,000 for direct and indirect costs and a fixed fee for a period normally not to exceed 1 year. *Note:* Phase I award levels and project periods are statutory guidelines. Therefore, applicants are encouraged to propose a budget and project period that are appropriate for completion of their research project. Deviations from the guidelines must be well justified.

R42 Small Business Technology Transfer (STTR) Grant—Phase II
Phase II STTR Grants (R42s) support in-depth development of cooperative research and development projects between research institutions and small, domestic, for-profit organizations. They are limited in time and amount, and applicants must have established during phase I their project's feasibility and potential for commercialization. Generally, support for Phase II awards may not exceed $500,000 for direct and indirect costs and a fixed fee for a period normally not to exceed 2 years. *Note:* Phase II award levels and project periods are statutory guidelines. Therefore, applicants are encouraged to propose a budget and project period that are appropriate for completion of the research project. Deviations from the guidelines must be well justified.

R43 Small Business Innovation Research (SBIR) Grant—Phase I
Phase I SBIR Grants (R43s) support research efforts by for-profit, domestic, small businesses. The objectives of this phase are to: (1) establish the technical merit and feasibility of proposed research or research and development (R&D) efforts, and (2) evaluate the performance of the small

Exhibit VIII. Summary of NCI Obligations by Mechanism, FY2010 (Dollars in Thousands)*†

		Number	Amount	% of Total
Research Project Grants	Non-Competing	3,619	1,536,844	30.2%
	Administrative Supplements	(254)	28,947	0.6%
	Competing	1,253	516,598	10.1%
	Subtotal, without SBIR/STTR Grants	4,872	2,082,389	40.9%
	SBIR/STTR Grants	207	85,669	1.7%
	Subtotal, Research Project Grants	**5,079**	**2,168,058**	**42.5%**
Centers & SPOREs	Cancer Centers Grants-P20/P30	66	295,856	5.8%
	SPOREs-P50	63	133,810	2.6%
	Other P50s/P20s	19	38,765	0.8%
	Other Specialized Centers	102	142,702	2.8%
	Subtotal, Centers	**250**	**611,133**	**12.0%**
Other Research	**Career Program**			
	Temin & Minority Mentored Awards-K01	77	10,823	0.2%
	Estab. Inv. Award-K05	21	3,134	0.1%
	Preventive Oncology-K07	97	13,278	0.3%
	Clinical Investigator-K08	83	12,408	0.2%
	Clinical Oncology-K12	18	12,922	0.3%
	Transitional Career Development-K22	30	4,963	0.1%
	Mentored Patient Oriented RCDA-K23	40	5,812	0.1%
	Mid-Career Invest. & Patient Orient. Res-K24	20	3,422	0.1%
	Mentored Quant. Res Career-K25	25	3,311	0.1%
	Inst. Curr. Award-K30	0	0	0.0%
	Pathway to Independence Awards-K99	41	4,841	0.1%
	Subtotal, Career Program	**452**	**74,914**	**1.5%**
	Cancer Education Program-R25	91	35,444	0.7%
	Clinical Cooperative Groups-U10	131	254,487	5.0%
	Minority Biomedical Support-S06	0	466	0.0%
	Res Enhancement-SC1 & Pilot Research-SC2	6	1,348	0.0%
	Continuing Education	6	685	0.0%
	Resource Grants-R24/U24	43	67,144	1.3%
	Explor Coop Agreement-U56	2	862	0.0%
	*Global Infect. Disease Rsrch Training Prog-D43	9	5,599	0.1%
	Conference Grants-R13	87	1,664	0.0%
	Subtotal, Other Research Grants	**827**	**442,613**	**8.7%**
Subtotal, Research Grants		**6,156**	**3,221,804**	**63.2%**
NRSA Fellowships	*Trainees:*	**1,428**	**67,564**	**1.3%**
R&D Contracts	R&D Contracts	399	588,742	11.6%
	SBIR Contracts	71	25,020	0.5%
	Subtotal, Contracts	**470**	**613,762**	**12.0%**
Intramural Research	Program		676,730	13.3%
	NIH Management Fund/SSF Assessment		128,602	2.5%
	Subtotal, Intramural Research *FTEs:*	**1,934**	**805,332**	**15.8%**
RMS	Research Mgmt and Support		345,412	6.8%
	NIH Management Fund/SSF Assessment		36,353	0.7%
	Subtotal, RMS *FTEs:*	**1,122**	**381,765**	**7.5%**
Buildings and Facilities			**7,920**	**0.2%**
Construction			**0**	**0.0%**
*Total NCI	*FTEs:*	3,056	5,098,147	100.0%

*Excludes projects awarded with Stamp Out Breast Cancer funds as well as royalty income.

†Source: *NCI Fact Book,* FY2010.

Exhibit IX. RPG Awards by Activity Code, FY2001-2010*† (Dollars in Thousands)

		R01	DP1	DP2	P01	R00	R35	R37	R29	RFA	U01	U19	R03	R21	R33	R15	R55	R56	SBIR/ STTR	TOTAL
2001	#	3,231			178		1	61	210	260	18		122	231	49	3	3		328	4,695
	$	1,008,199			301,115		2,186	26,682	23,738	150,224	14,873		9,024	42,326	23,883	358	300		75,833	1,678,741
2002	#	3,376			173			65	112	267	17		186	308	79	10	9		374	4,976
	$	1,093,908			317,632			29,445	12,471	177,195	17,531		14,115	57,633	39,317	1,477	850		86,367	1,847,941
2003	#	3,573			178			70	14	252	27		203	360	81	21			356	5,135
	$	1,207,387			336,607			35,360	1,584	173,342	31,126		15,207	67,742	37,714	3,086			90,857	2,000,012
2004	#	3,780			177			73	0	233	26		240	425	96	20			397	5,467
	$	1,277,185			344,489			37,888	53	168,539	31,377		18,067	77,970	42,931	4,560			99,579	2,102,638
2005	#	3,848			176			74		254	30	1	223	430	88	20	2	1	265	5,412
	$	1,312,762			338,660			40,007		171,403	34,100	1,049	16,894	76,566	36,250	4,091	200	407	97,775	2,130,164
2006	#	3,909			173			76		273	26	3	218	405	73	14		2	263	5,435
	$	1,293,880			339,616			40,067		173,304	31,292	4,365	16,558	70,650	28,726	2,983		649	96,055	2,098,145
2007	#	3,849			172			73		285	22	3	284	437	48	19		2	278	5,472
	$	1,266,622			326,968			38,232		177,423	24,295	4,212	21,640	78,748	16,739	4,042		495	93,677	2,053,093
2008	#	3,732	2		158	2		70		294	25	3	256	466	36	22		2	312	5,380
	$	1,250,346	1,651		305,250	497		36,287		174,254	20,872	4,366	19,597	92,120	13,770	4,725		302	97,439	2,021,476
2009	#	3,573	3		151	29		63		326	32	2	239	447	25	27	1	0	261	5,179
	$	1,248,939	3,313		302,270	7,186		32,640		218,798	31,320	1,584	18,401	91,537	9,094	5,823	100	79	91,954	2,063,038
2010	#	3,655	5	1	140	55		61		275	43	1	181	415	16	24			207	5,079
	$	1,323,673	6,021	2,512	280,531	13,665		31,498		200,424	36,209	1,252	14,195	83,950	5,583	7,539		8	85,669	2,092,729

Research Project Grants and Dollars Awarded FY2001-2010*

*Excludes projects awarded with the Stamp Out Breast Cancer Funds and Program Evaluation.

†Source: *NCI Fact Book,* FY2010.

business awardee organization prior to providing further Federal support in Phase II (R44). Generally, support for Phase I awards may not exceed $100,000 for direct and indirect costs and a fixed fee for a period normally not to exceed 6 months. ***Note:*** Phase I award levels and project periods are statutory guidelines. Therefore, applicants are encouraged to propose a budget and project period that are appropriate for completion of the research project. Deviations from the guidelines must be well justified.

R44 Small Business Innovation Research (SBIR) Grant—Phase II
Phase II SBIR Grants (R44s) continue those R&D efforts that were started in Phase I (R43). Awards are based on the results of Phase I and the scientific and technical merit and commercial potential of the Phase II application. Only Phase I awardees are eligible for Phase II. Generally, support for Phase II may not exceed $750,000 for direct and indirect costs and a fixed fee for a period normally not to exceed 2 years. ***Note:*** Phase II award levels and project periods are statutory guidelines. Therefore, applicants are encouraged to propose a budget and project period that are appropriate for completion of the research project. Deviations from the guidelines must be well justified.

R55 James A. Shannon Director's Award
Applicants do not submit requests for Shannon Awards (R55). Instead, NCI program staff nominate previously reviewed R01 and R03 applications that are beyond the current NCI payline but, because of their merit, are eligible for funding. After each of the three review cycles per year, Shannon Award nominees are administratively reviewed by the NCI according to standard review criteria, then submitted to the Office of Extramural Research, NIH, for expedited review and concurrence prior to funding.

Shannon Awards (R55s) provide a limited award to investigators to further develop, test, and refine research techniques; perform secondary analysis of available data sets; test the feasibility of innovative and creative approaches; and conduct other discrete projects that can demonstrate the investigator's research capabilities and lend additional weight to his or her already meritorious application.

R56 High Priority, Short-Term Project Award
Applicants do not submit requests for a High Priority Award (R56). Instead, NCI program staff nominate previously reviewed R01 applications that are beyond the current NCI payline but, because of their merit, are eligible for funding. After each of the three review cycles per year, High Priority nominees are administratively reviewed by the NCI according to standard review criteria. The NCI then determines whether any awards are made from NCI funds.

High Priority Awards (R56s) provide limited, interim support to enable an applicant to gather additional data for revision of a new or competing renewal application. The R56 will assist early career stage scientists trying to establish research careers as well as more experienced scientists who just missed receiving funds.

II. Cancer Centers and Specialized Programs of Research Excellence

The Cancer Centers, SPORE Program, and other specialized centers contain a great diversity of research approaches. In FY2010, expenditures totaled about $611 million, accounting for 12 percent of the total NCI budget.

P20 Planning Grant
Planning Grants (P20s) support planning for new programs, expansion or modification of existing resources, and feasibility studies for new approaches. Such awards have been particularly useful in the development of Cancer Centers and SPOREs but are no longer available for Cancer Centers.

P30 Cancer Center Support Grant
Cancer Center Support Grants (P30s) provide support primarily for the research infrastructure of an active and unified Cancer Center, for the purpose of: consolidating and focusing cancer-related activities; increasing research productivity; promoting shared use of research resources and improved quality control; stimulating and promoting interdisciplinary and collaborative research; and increasing the rate at which research discoveries are translated into medical developments.

P50 Specialized Center Grant
Specialized Center Grants (P50s) support any part of the full range of R&D, from very basic to clinical activities. They also may support ancillary activities, such as the protracted patient care that may be necessary while conducting primary research or R&D. The spectrum of activities comprises a multidisciplinary attack on cancer. These grants differ from Program Project Grants in that they usually are developed in response to an announcement of the programmatic needs of the NCI and receive continuous attention from its staff. Centers

also may serve as regional or national resources for special research purposes.

The Specialized Programs of Research Excellence (SPORE) grant is one type of Specialized Center. The NCI SPORE is an organ site application, which includes basic and clinical investigation, thus having a significant translational component.

U54 Specialized Center – Cooperative Agreement
(see Cooperative Agreement Section)

U56 Exploratory Grant – Cooperative Agreement
(see Cooperative Agreement Section)

III. Other Research Grants

Other research grants include the Research Career Program and all other research grants not included in Research Project Grants, Research Centers, and/or Cancer Prevention and Control, except for National Research Service Awards. The NCI Research Career Program includes all "K" awards. Other research grants also include the Clinical Cooperative Groups, Cancer Education Program (R25), resource grants (R24/U24), conference grants, and exploratory cooperative agreements (U56). In FY2010, other research expenditures totaled approximately $442 million, accounting for 8.7 percent of the total NCI budget.

IV. Career Awards and Cancer Education

K01 Mentored Research Scientist Development Award
Mentored Research Scientist Development Awards (K01s) provide support and "protected time" for an intensive, supervised career development experience in the biomedical, behavioral, or clinical sciences leading to research independence. Some Institutes/Centers use the K01 to support individuals who propose to train in a new field; for individuals who have had a hiatus in their research career; or to increase research workforce diversity. The NCI supports the Mentored Research Scientist Development Award to Support Diversity.

K05 Senior Scientist Award
Senior Scientist Awards (K05s) support outstanding established scientists who have demonstrated a sustained, high level of productivity, research accomplishments, and contributions to research in the fields of cancer prevention, control, and population sciences. These awards provide protected time to devote to research and to act as mentors for young investigators. NCI supports the Established Investigator Award in Cancer Prevention, Control, Behavioral, and Population Sciences Research.

K07 Academic Career Award
Academic Career Awards (K07s) support more junior candidates who are interested in developing academic and research expertise in a specific area. They also support more senior individuals with acknowledged scientific expertise and leadership skills who are interested in improving the curricula and enhancing the research capability within an academic institution. NCI supports the Cancer Prevention, Control, Behavioral and Population Sciences Career Development Award.

K08 Mentored Clinical Scientist Development Award
Mentored Clinical Scientist Development Awards (K08s) support the development of outstanding clinical research scientists. These awards provide specialized study for clinically trained professionals who are committed to a career in research and have the potential to develop into independent investigators. The NCI supports two K08 awards: the Mentored Clinical Scientist Development Award and the Mentored Clinical Scientist Development Award to Promote Diversity.

K12 Mentored Clinical Scientist Development Program Award
Mentored Clinical Scientist Development Program Awards (K12s) help newly trained, appointed clinicians gain independent research skills and experience in a fundamental science within the framework of an interdisciplinary R&D program. NCI supports the Paul Calabresi Award for Clinical Oncology.

K18 Career Enhancement Award for Stem Cell Research
This program encourages investigators to obtain the training and career development they need to appropriately use stem cells in their research. It is intended to enable investigators to change the direction of their research careers or to take time from their regular professional responsibilities to broaden their scientific background by acquiring new research capabilities, specifically in the use of human or animal embryonic, adult, or cord blood stem cells. The award includes salary and support for career development costs.

K22 Career Transition Award
Career Transition Awards (K22s) help newly trained basic or clinical investigators to develop their independent research skills through a two-phase program: an initial period involving an intramural appointment at the NIH and a final period of support at an extramural institution. The award is intended to enable the investigator to establish a record of independent research to

sustain or promote a successful research career. The NCI supports two K22 awards: the Scholars Program and the Transition Career Development Award. The NCI Scholars Program provides an opportunity for outstanding new investigators to begin independent research careers, intramurally, within the special environment of the NCI. It then enables awardees to continue their careers extramurally at an institution of their choice, where they are appointed to junior faculty positions or the equivalent. The NCI Transition Career Development Award is a fully portable mechanism that facilitates the professional advancement of talented clinician cancer scientists, clinicians in patient-oriented cancer research, and researchers in cancer prevention, control, and the population sciences.

K23 Mentored Patient-Oriented Research Career Development Award
Mentored Patient-Oriented Research Career Development Awards (K23s) provide support for the career development of investigators who focus their research endeavors on patient-oriented research. The mechanism provides support for a period of supervised study and research to clinically trained professionals who have the potential to develop into productive clinical investigators in patient-oriented research.

K24 Mid-Career Investigator in Patient-Oriented Research Award
Mid-Career Investigator in Patient-Oriented Research Awards (K24s) provide clinicians the opportunity to dedicate time to patient-oriented research and to mentor other clinical investigators in patient-oriented research.

K25 Mentored Quantitative Research Career Development Award
Mentored Quantitative Research Career Development Awards (K25s) support the career development of investigators with quantitative scientific and engineering backgrounds outside of biology or medicine, who have made a commitment to focus their research endeavors on behavioral and biomedical research (basic or clinical).

K30 Institutional Curriculum Award
Institutional Curriculum Awards (K30s) support the development, conduct, and evaluation of curricula that are designed to improve the quality of training for aspiring clinical investigators.

K99/R00 Howard Temin Pathway to Independence Awards in Cancer Research
Howard Temin Pathway to Independence Awards in Cancer Research (K99/R00) support highly promising, postdoctoral research scientists. The initial phase is followed by independent support contingent on securing an independent research position. The goal of this award is to facilitate an investigator receiving an R01 award earlier in his/her research career.

V. Training (NRSA)

The National Research Service Award (NRSA) is the major mechanism providing long-term, stable support to a wide range of promising scientists and research clinicians. FY2010 NRSA expenditures totaled approximately $67.5 million, accounting for 1.3 percent of the NCI budget.

F31 Predoctoral Individual National Research Service Award
Predoctoral Individual National Research Service Awards (F31s) provide predoctoral individuals with supervised research training in specified health and health-related areas leading toward a research degree (e.g., Ph.D.).

F32 Postdoctoral Individual National Research Service Award
Postdoctoral Individual National Research Service Awards (F32s) provide postdoctoral research training to individuals to broaden their scientific background and extend their potential for research in specified, health-related areas.

F33 National Research Service Award for Senior Fellows
National Research Service Awards for Senior Fellows (F33s) enable experienced scientists to take time away from their regular professional responsibilities to: make major changes in the direction of research careers; broaden scientific background; acquire new research capabilities; enlarge command of an allied research field; or increase capabilities to engage in health-related research.

T32 Institutional National Research Service Award
Institutional National Research Service Awards (T32s) support training opportunities at the predoctoral or postdoctoral level at qualified institutions. Applicants must have the staff and facilities for the proposed program. After the award is made, the institution's training Program Director is responsible for selecting the trainees and for administering the program. This program does not support residencies.

D43 International Training Grants in Epidemiology
To improve and expand epidemiologic research and the utilization of epidemiology in clinical tri-

als and prevention research in foreign countries through support of training programs for foreign health professionals, technicians, and other health care workers.

DP1 NIH Director's Pioneer Award (NDPA)
To support individuals who have the potential to make extraordinary contributions to medical research. The NIH Director's Pioneer Award is not renewable.

DP2 NIH Director's New Innovator Awards
To support highly innovative research projects by new investigators in all areas of biomedical and behavioral research.

Other Grant Mechanisms

R13 Conference Grant
Conference Grants (R13s) support national or international meetings, conferences, and workshops that are of value in promoting the goals of the National Cancer Program.

R15 Academic Research Enhancement Award (AREA)
Academic Research Enhancement Award (AREA) Grants (R15s) support small-scale research projects conducted by faculty in primarily baccalaureate degree-granting domestic institutions. Awards are for up to $75,000 in direct costs (plus applicable indirect costs) for periods not to exceed 36 months.

R24 Resource-Related Research Project
Resource-Related Research Project Grants (R24s) support research projects that will enhance the capability of resources to serve biomedical research.

R25 Cancer Education Grant
Cancer Education Grants (R25s) support the development and implementation of programs related to education, information provision, training, technical assistance, coordination, or evaluation. The NCI supports two distinct Cancer Education programs: the Cancer Education and Career Development Program, and the Cancer Education Grant Program (CEGP). The NCI Cancer Education and Career Development Program (R25T) is an institutional grant program that supports the development and implementation of curriculum-dependent programs to train predoctoral and postdoctoral candidates in cancer research settings that are highly interdisciplinary and collaborative. The NCI CEGP is a flexible, curriculum-driven program aimed at developing and sustaining innovative educational approaches that ultimately will reduce cancer incidence, mortality, and morbidity. The program also focuses on improving the quality of life for cancer patients. The CEGP awards (R25Es) address a need that is not fulfilled adequately by any other grant mechanism available at the NIH. These awards are dedicated to areas of particular concern by the NCI.

S06 Minority Biomedical Research Support (MBRS)
Minority Biomedical Research Support Grants (S06s) provide funds to strengthen the biomedical research and research training capability of ethnic minority institutions, thus creating a more favorable milieu for increasing the involvement of minority faculty and students in biomedical research.

S21 Research and Institutional Resources Health Disparities Endowment Grants – Capacity Building
To strengthen the research and training infrastructure of the institution, while addressing current and emerging needs in minority health and other health disparities research.

SC1 Research Enhancement Award
Individual investigator-initiated research projects aimed at developing researchers at minority-serving institutions (MSIs) to a stage where they can transition successfully to other extramural support (R01 or equivalent).

SC2 Pilot Research Project
Individual investigator-initiated pilot research projects for faculty at MSIs to generate preliminary data for a more ambitious research project.

Cooperative Agreements

The cooperative agreement is a mechanism to provide funding assistance for a variety of activities. The Federal Grant and Cooperative Agreement Act of 1977 authorized use of the cooperative agreement and formally defined the circumstances under which this mechanism is to be employed by Federal agencies. These instruments are used for situations in which an assistance relationship will exist between the NCI and a recipient and substantial programmatic involvement is anticipated.

U01 Research Project Cooperative Agreement
Research Project Cooperative Agreements (U01s) support discrete, specified, circumscribed projects to be performed by the named investigator(s) in an area representing his/her specific interest and competencies. This mechanism is utilized when substantial programmatic involvement is anticipated between the NCI and the recipient.

U10 Clinical Research Cooperative Agreement (Clinical Cooperative Groups)
Clinical Research Cooperative Agreements (U10s) support clinical evaluations of various methods of therapy and/or prevention in specific disease areas. These represent cooperative programs between sponsoring institutions and participating principal investigators, and usually are conducted under established protocols.

U13 Conference Cooperative Agreement
Conference Cooperative Agreements (U13s) support international, national, or regional meetings, conferences, and workshops for which substantial programmatic NCI staff involvement is planned to assist the recipients.

U19 Research Program Cooperative Agreement
Research Program Cooperative Agreements (U19s) support research programs that have multiple projects directed toward a specific major objective, basic theme, or program goal, requiring a broadly based, multidisciplinary, and often long-term approach. Substantial Federal programmatic staff involvement is intended to assist investigators during performance of research activities, as defined in the terms and conditions of the award. This mechanism can provide support for certain basic, shared resources, which facilitate the total research effort, including clinical components.

U24 Resource-Related Research Project Cooperative Agreement
Resource-Related Research Project Cooperative Agreements (U24s) support projects that help improve the capability of resources to serve biomedical research.

U43 Small Business Innovation Research (SBIR) Cooperative Agreement—Phase I (see R43)
Phase I SBIR Cooperative Agreements (U43s) support finite projects to establish the technical merit and feasibility of R&D ideas that ultimately may lead to the development of commercial products or services. This mechanism is utilized when an assistance relationship will exist between the NCI and a recipient and in which substantial programmatic involvement is anticipated. Cooperative agreement applications are considered only for the topics specifically listed in the current SBIR Omnibus Solicitation. *Note:* Phase I award levels and project periods are statutory guidelines. Applicants are encouraged to propose a budget and project period that are appropriate for completion of the research project. Deviations from the guidelines must be well justified.

U44 Small Business Innovation Research (SBIR) Cooperative Agreement—Phase II (see U43 and R44)
Phase II SBIR Cooperative Agreements (U44s) support in-depth development of R&D ideas for which feasibility has been established in Phase I (U43) and that are likely to result in commercial products or services. *Note:* Phase II award levels and project periods are statutory guidelines. Applicants are encouraged to propose a budget and project period that are appropriate for completion of the research project. Deviations from the guidelines must be well justified.

U54 Specialized Center—Cooperative Agreement
Specialized Center Cooperative Agreements (U54s) support any part of the full range of R&D, from basic concepts to clinical applications. The U54 may involve ancillary supportive activities, such as the provision of protracted patient care during the primary research or R&D effort. The spectrum of activities comprises a multidisciplinary attack on a specific disease entity or biomedical problem area. The U54s differ from program projects in that they usually are developed in response to an announcement of the programmatic needs of an Institute or division and subsequently receive continuous attention from its staff. Centers also may serve as regional or national resources for special research purposes, with funding staff helping to identify appropriate priority needs. At the NCI, U54s support comprehensive partnerships between Minority Serving Institutions (MSIs) and the NCI-designated Cancer Centers, for the benefit of both. These partnerships focus on cancer research career development at the MSI or cancer research plus one or more target areas in cancer research training. These partnerships also may focus on cancer research and target areas in cancer education for, or cancer outreach to, minority communities.

U56 Exploratory Grant—Cooperative Agreement
Exploratory Grant Cooperative Agreements (U56s) support planning for new programs, expansion or modification of existing resources, and development of feasibility studies to explore 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. Substantial Federal programmatic staff involvement is intended to assist investigators during the performance of the research activities, as defined in the terms and conditions of award.

Solicitation of Grant Applications

Electronic grant applications must be submitted in response to a Funding Opportunity Announcement (FOA) published on www.grants.gov or the *NIH Guide for Grants and Contracts*. "Investigator Initiated" or "unsolicited" applications are submitted to Parent Announcements that are mechanism (e.g. R01, R21, R44, etc.) specific. In addition, the NCI may encourage the submission of grant applications through the publication of additional FOAs using the following types of solicitations:

Program Announcements (PAs)
PAs describe continuing, new, or expanded program interests for which grant or cooperative agreement applications are invited. Applications in response to PAs are reviewed in the same manner as unsolicited grant applications (i.e., by chartered peer review committees or Special Emphasis Panels (SEPs) of the Center for Scientific Review [CSR] or by the NCI).

Program Announcements with Special Receipt/ Review (PARs)
PARs are program announcements that contain special receipt dates, referral guidelines, and review considerations and are reviewed either by CSR or by a specific Institute's IRG or SEP with funds earmarked for the initiative.

Requests for Applications (RFAs)
RFAs are issued to invite grant or cooperative agreement applications in a well-defined scientific area, to stimulate activity in NCI programmatic priority areas. Usually a single application receipt date is specified, and the announcement identifies the amount of funds earmarked for the initiative and the number of awards likely to be funded. Applications are evaluated before review for responsiveness to the RFA. Applications received in response to a particular RFA are reviewed by an appropriate NCI Special Emphasis Panel (SEP).

All PAs and RFAs are published in the *NIH Guide for Grants and Contracts* (http://www.nih.gov/grants/guide/index.html) and, when appropriate, in scientific journals and periodicals.

Contracts

Research and Development Contracts

To stimulate scientific inquiry, direct it toward promising areas of current research, and solve specific research problems, the NCI awards research, development, demonstration, and support contracts to both nonprofit and commercial organizations. The idea for a contract may be generated by the NCI program staff (usually the Project Officer), or it may originate from members of the scientific community. The negotiated contract used by the NCI is awarded through a competitive process, in which bidders are judged on the basis of technical (scientific merit), business, and cost factors. The responsibility for reviewing the technical merit of proposals for R&D contracts is lodged in the Special Review and Logistics Branch (SRLB), DEA, NCI. Review responsibility is separated from those responsibilities of the Project and Contracting Officers. After award, the NCI is substantially involved in monitoring the project; this may range from tight control to general surveillance and support. Contracts may be used in support of either research or resource projects. In a research contract, the NCI defines the specific area of research and may identify general approaches. Such a contract usually is used to stimulate work in an area that has been neglected by the private sector.

Loan Repayment Program (LRP)

The LRP was started in 1989 to recruit and retain highly qualified professionals as AIDS researchers. Using the contract mechanism, this program provides for repayment of up to $35,000 (principal and interest) of eligible, educational loans for qualified clinical and pediatric investigators, for each year of their research service. To be eligible, the awardee must agree to engage in clinical or pediatric research for a minimum of 2 years. Originally confined to intramural researchers, the LRP was expanded in 2002 to include extramural investigators.

L30 Clinical Research Loan Repayment Program
The Clinical Research Loan Repayment Program is for eligible investigators, in exchange for a 2-year commitment to clinical research. To participate in the program, individuals must hold an appropriate terminal degree from an accredited institution, must conduct research for 20 hours per week (based on a 40-hour week), and must conduct research that is supported by a domestic, nonprofit institution or by a U.S. Government entity.

L40 Pediatric Research Loan Repayment Program
The Pediatric Research Loan Repayment Program is for eligible investigators, in exchange for a 2-year commitment to pediatric research. To participate in the program, individuals must hold an appropriate terminal degree from an accredited institution, must conduct research for 20 hours per week (based on a 40-hour week), and must conduct research that is supported by a domestic, nonprofit institution or by a U.S. Government entity.

PEER REVIEW

INTRODUCTION

Because of the magnitude, diversity, and complexity of its research mission, as well as its pursuit of excellence, the National Institutes of Health (NIH) draws on a national pool of scientists actively engaged in research. These scientists advise the NIH about how to select research projects based on scientific merit.

As discussed in the previous section, the National Cancer Institute (NCI) supports research through three major mechanisms: investigator-initiated projects, cooperative agreements for projects in which programmatic involvement between the NCI and a recipient is anticipated, and research and development contracts for projects that are undertaken in response to NCI Requests for Proposals (RFP).

The Board of Scientific Advisors performs the review of concepts for special initiatives, including both Requests for Applications (RFA) for grants and cooperative agreements and RFPs for R&D contracts and master agreements. All undergo peer review before funding decisions are made.

The dual peer review system of the NIH consists of two sequential levels of review, mandated by statute. Although the system already had been in effect for many years, the first or initial level of peer review of research grant applications was formally mandated in 1974 by Section 475 of the Public Health Service Act. The review of grant applications by national boards/councils was mandated by the National Cancer Act in 1937, and incorporated into the Public Health Service Act in 1944. In 1978, P.L. 95-224 authorized and directed the use of cooperative agreements, which also are subject to peer review.

The National Cancer Advisory Board (NCAB) performs the second level of review for NCI grants, as mandated by the National Cancer Act of 1937 and incorporated into the Public Health Service Act in 1944. NCAB members bring to the grant review process their knowledge in each of the relevant programmatic areas. They also are familiar with the NCI priorities and procedures and are aware of the missions of the diverse Institutes in biomedical research as well as the health needs of the American people.

A board or council, hereafter referred to as board, is composed of both scientific and lay public representatives who are selected for their expertise, interest, or activity in matters related to the mission of the specific Institute for which the board or council serves. Board recommendations are based not only on consideration of scientific merit as judged by the CSR Integrated Review Groups (IRGs) or the NCI Initial Review Group (IRG) or Special Emphasis Panel (SEP), but also on the relevance of the proposed study to an Institute's programs and priorities. By statute, Congress established the National Advisory Cancer Council as the National Cancer Advisory Board.

The dual review system—which separates the scientific assessment of proposed projects from policy decisions about scientific areas to be supported and the level of resources to be allocated—permits a more objective evaluation than would a single level of peer review. It guarantees that the NCI program staff will assess only the programmatic aspects of an application, while the members of the scientific research community evaluate the project's technical merit. This dual system provides the responsible NIH official with the best advice available regarding both scientific and societal values and needs.

The following describes the review of grant applications in detail. Review of contract proposals is described on pp. 34-35.

SUBMISSION OF GRANT APPLICATIONS

Grants and cooperative agreement applications may be submitted by nonprofit and for-profit organizations, institutions of higher education, hospitals, research foundations, governments and their agencies in response to Funding Opportunity Announcements (FOA). An FOA is a publicly available document by which a Federal agency makes known its intentions to award discretionary grants or cooperative agreements, usually as a result of competition for funds. FOAs may be known as Program Announcements, Requests for Applications, solicitations, or other names depending on the agency and type of program. FOAs can be found at http://grants.nih.gov/grants/guide/ and in the *NIH Guide for Grants and Contracts*. In addition,

the NIH and other HHS Agencies have developed omnibus Parent Announcements for common grant mechanisms (e.g., R01, R03, R43, etc.) that have transitioned to electronic submission, for use by applicants who wish to submit what were formerly termed "unsolicited" or "investigator-initiated" applications.

The process of developing a grant application usually begins with the Principal Investigator (PI) who initiates the research data and prepares the application. The PI should work concurrently with the authorized business official from his/her institution to ensure that all of the application requirements are met. The PI accepts responsibility for the scientific conduct of the project and submission of progress and any other required reports. The applicant institution is in turn legally responsible and accountable to the NIH for the performance and financial aspects of the grant-supported
activity.

ELECTRONIC SUBMISSION OF GRANT APPLICATIONS

The National Institutes of Health is transitioning from paper submission of grant applications to electronic submission via the Web portal of http://www.Grants.gov, while simultaneously phasing out the PHS398 grant application form and replacing it with the SF424 [Research and Research-related (R&R)] application. This staged transition began in December 2005. The majority of single component grant mechanisms have transitioned to electronic submissions. Multi-component grant applications and cooperative agreements should transition in the next few years. Electronic submissions must be submitted in response to a Funding Opportunity Announcement (FOA) and involve two separate systems working together – Grants.gov and eRA Commons. The applicant institution must be registered in Grants.gov and the authorized business official is responsible for submission of electronic applications. The applicant institution is responsible for submission through Grants.gov.

PROCESSING OF GRANT APPLICATIONS

Receipt and Review Assignment of Grant Applications

The referral section of the Center for Scientific Review (CSR) serves as the central receipt point for all competing applications, including applications submitted in response to specifically targeted, pre-announced RFAs or program announcements in areas of Institute interest. Exhibit X illustrates a typical grants process from the date of receipt of applications through assignment of applications. Within CSR's Division of Receipt and Referral, referral officers, who are Health Scientist Administrators, determine the relevance of the applications to NIH's overall mission and assign each acceptable application to an appropriate CSR IRG or an Institute for peer review. The choice of an IRG is based on the relevance of a proposed research project to the review responsibilities of the IRG members. Most NIH Institutes, including the NCI, have established their own review units to review specialized grant applications of high programmatic interest, such as those related to Cancer Control, Cancer Centers, Clinical Cooperative Groups, National Research Service Awards, Clinical Cancer Education Programs, Program Projects, and RFAs and special Program Announcements.

Institute/Center (IC) and Program Assignment

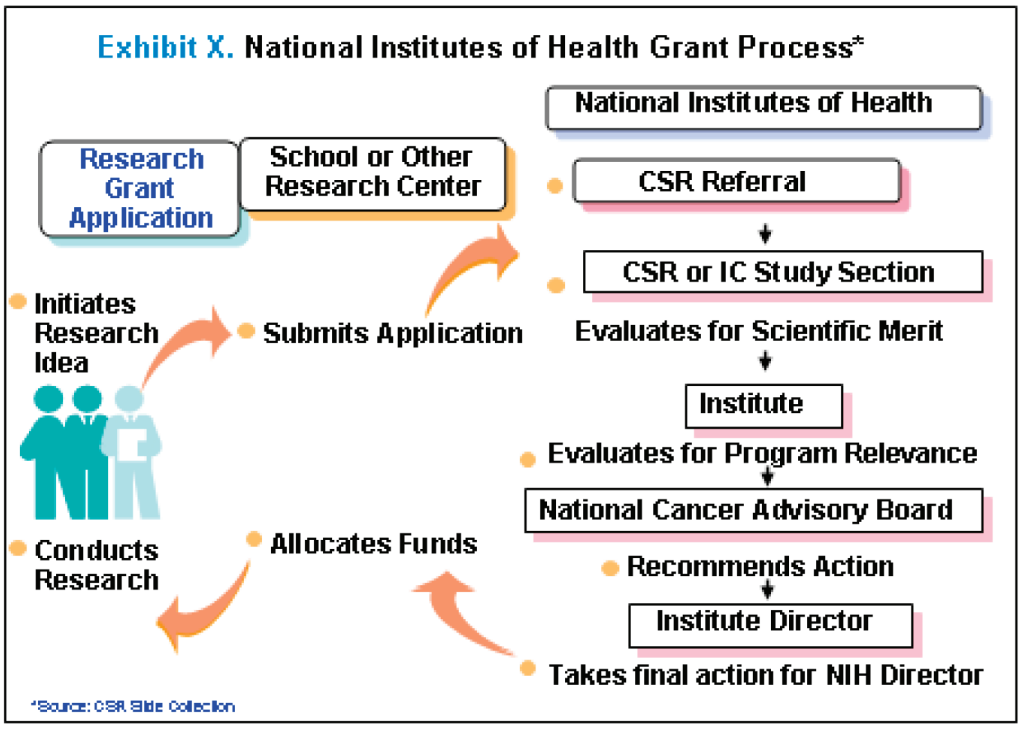
CSR also assigns each application to an IC based on that Institute's legislatively mandated program responsibility using negotiated criteria (referral guidelines). If the subject matter of an application is pertinent to the missions of two Institutes, a dual assignment may be made. Then, the NCI Referral Office refers all applications assigned to the NCI by CSR to one of the 45 NCI extramural research program areas. The NCI Referral Office staff assigns all incoming applications, tracks their review status, and distributes them to the appropriate NCI Program Director. In FY2010, 13,935 grant applications were received for referral.

INITIAL PEER REVIEW

CSR Integrated Review Groups

There are approximately 25 chartered IRGs distributed among the five review divisions within the CSR. Each IRG is administered by a Scientific Review Officer (SRO) and has 5 to 10 Scientific Review Groups (SRGs), or "study sections," that review applications on specific topics (e.g., cell biology, clinical oncology, pathology, biochemistry, virology), regardless of the awarding NIH Institute assignment. There are approximately 184 regular study sections in the 25 IRGs, plus 33 fellowship and 37 small business Special Emphasis Panels (SEPs). A listing of IRGs and their study

Exhibit X. National Institutes of Health Grant Process*



sections may be found at the following Web site: http://cms.csr.nih.gov/PeerReviewMeetings/csrirgdescriptionnew/.

Generally, a study section is composed of 12 to 18 mostly non-Federal scientists who are selected on the basis of recognized competence in their respective research fields. In each of the three review cycles per year, a CSR study section may review between 50 and 100 grant applications.

Each study section is organized and managed by an SRO—an NIH staff scientist who is the designated Federal official responsible for ensuring that the grant applications are reviewed in an impartial environment. SROs are responsible for overseeing the scientific peer review of applications. Their major responsibilities include managing study section meetings, nominating study section members, selecting *ad hoc* reviewers and site visitors, providing orientation for members of review groups, explaining and interpreting the NIH review policies and procedures, managing project site visits and study section meetings (and sometimes site visits), and preparing Summary Statements. They also are responsible for attending advisory board or council meetings to provide requested information in support of the peer review committee recommendations; communicating with program staff on review issues; and discussing review issues and policies with applicants. SROs do not have continuing programmatic, scientific, or fiscal responsibilities for the applications after the scientific peer review is completed.

NCI Review of Grant Applications

The NCI conducts its own initial review of certain specialized or complex cancer-oriented applications, including Research Program Projects, Cancer Center Support Grants, Cooperative Clinical Research Grants, Conference Activities, Research Demonstration and Dissemination Projects, SPOREs, SBIRs, and others. These reviews are conducted by either NCI chartered or *ad hoc* SEP peer review committees, which may include from 15 to 80 reviewers. In FY2010, the DEA reviewed 2,146 grant and cooperative agreement applications.

Four branches are responsible for organizing, managing, and reporting the scientific peer review of applications for a wide variety of grant mechanisms: the Research Programs Review Branch (RPRB), the Special Review and Logistics Branch (SRLB), the Resources and Training Review Branch (RTRB), and the Program Coordination and Referral Branch (PCRB).

The RTRB has primary responsibility for reviewing applications for Cancer Centers, cancer train-

ing and career development, and the NCI Clinical Trials Cooperative Groups using five standing IRG subcommittees. Cancer Centers reviews involve site visits with subsequent review by the appropriate parent committees.

The RPRB has primary responsibility for reviewing unsolicited P01s and applications for SPOREs (P50) in various organ sites with Special Emphasis Panels (SEPs). The SRLB is responsible for the review of most applications submitted in response to the initiatives published by the Institute, including RFAs, PAs, and RFPs. All of these reviews are conducted by SEPs and include the following types of mechanisms: P50, R03, U19, U54, U56, SBIRs (R43s and R44s), and STTRs (R41s and R42s). For RFAs, the size and composition of the SEP is dependent on the research scope and number of applications submitted in response to the special initiative. The PCRB provides review support for several grant applications, including conference grants (R13).

The various committees are responsible for advising the NCI Director and the NCAB concerning the scientific and technical merit of grant applications assigned to the NCI for the initial review, which addresses each application's scientific merit in terms of its discipline and the clinical implications of its research protocol. This review is conducted according to the established NIH procedures. With the exception of the parent committees used to review NCI Clinical Trials Cooperative Groups and Cancer Centers, Summary Statements are prepared in the same general format that is used by the CSR.

Once a grant application receives an NCI program assignment, an NCI Program Director follows its progress through the review process and, if an award is made, through the post-award period. For the duration of that project period, the Program Director is the contact point, negotiator, advisor, and advocate for the principal investigator. This individual evaluates the relevance of the research, considers the appropriateness of the appraisal by the study section, and makes recommendations to the NCAB regarding any need for special action in a particular case.

The Review Session

IRGs (CSR study sections and NCI review committees) and SEPs meet from 1 to 3 months before each meeting of the National Cancer Advisory Board (NCAB). Before the meeting, the SRO of the IRG studies all of the applications assigned to his or her committee and obtains any additional information necessary for the review from the principal investigators or applicant institutions.

Approximately 6 to 8 weeks before the meeting date, the SRO assigns each application to two or more members of the IRG, who prepare detailed critiques and lead the discussion of the application at the review meeting. Each member reviews approximately 10 or more applications in detail. In addition, every member is expected to read and comment on as many applications as possible to be reviewed at the meeting. During the three annual meetings, each of which lasts 2 to 3 days, each IRG reviews approximately 85 applications.

The SRO is responsible for providing any information or materials necessary for the review, communicating with applicants, and providing the appropriate I/C advisory board/council with an accurate record of the proceedings in the form of a detailed summary statement. At the review meeting, each assigned reviewer makes an initial recommendation to the review group about the merit of each application. A discussion ensues, following which each member of the committee votes on the application's technical merit and assigns an overall impact/priority score. Scores are summed and averaged for each application. The CSR meeting is presided over by the chairperson, who is a member of the IRG, nominated by the SRO and appointed by the Director of the NIH. The NCI DEA Director has the authority to appoint NCI IRG members and chairpersons.

The IRG meetings also are attended by staff members of ICs to which applications have been assigned, liaison members for certain other Federal agencies, and appropriate NIH staff. The review of applications is conducted in closed sessions, which are attended only by review committee members and appropriate Institute staff.

Study Section Recommendations

At present, the possible recommendations by the review committee are: scoring, not discussed (ND), not recommended for further consideration (NR), or deferral (DF). If an application has significant and substantial scientific merit, it is given a priority score from 1 to 9 and, in the case of CSR-reviewed applications, a percentile ranking is calculated for the application. In the streamlined review process implemented at the NIH (particularly for single-project applications), the reviewers identify but do not discuss or score applications that are not in the upper half of the applications being reviewed by that committee for that round. For reviews of applications received in response to an RFA, the reviewers may be asked to identify the applications that are not in the upper half of the group of applications under review. Review-

ers' critiques of ND applications are provided as feedback to grant applicants. An application may be designated Not Recommended for Further Consideration (NR) if it lacks significant and substantial merit; presents serious ethical problems in the protection of human subjects from research risks; or presents serious ethical problems in the use of vertebrate animals, biohazards, and/or select agents. Applications designated as NR or ND do not proceed to the second level of peer review (National Advisory Council/Board). An action for scoring is equivalent to a recommendation that a grant be awarded, provided that sufficient funds are available.

Summary Statements

Immediately after the IRG meeting, the SRO prepares individual reports summarizing the recommendation for each application, called Summary Statements. Before the three annual grant review meetings, copies of Summary Statements are posted on the Web as part of the Electronic Council Book. Before the NCAB meets, applicants routinely are provided with copies of their own Summary Statements by accessing the document using the NIH Electronic Research Administration Commons.

Post NCAB Meetings and Funding Decisions

After each NCAB meeting, NCI staff members meet to discuss and review the NCAB's recommendations. The NCI SPL determines the paylines for the different grant mechanisms and approves the funding plans for all RFAs and other special initiatives. Applicants who will be funded are subsequently notified at the time of the award negotiation. Ideally, approximately 8 to 9 months will have elapsed since the principal investigator submitted the application.

REVIEW OF CONTRACT PROPOSALS

The NCAB has no direct involvement with the Research and Development (R&D) contract program of the NCI; R&D contract concepts are reviewed by the BSA.

The contract solicitation process begins when an NCI program staff member (usually the individual who will become the Project Officer) develops a concept for a contract project through personal initiative, discussion with advisory groups, consultation with others in the program, and/or interactions with members of the scientific community. The relevance, priority, and need for the anticipated project are assessed by NCI program staff, and the concept is subjected to a series of internal clearances, including review by the Scientific Program Leadership (SPL) of the NCI. Federal regulations (the 1974 Amendments to the National Cancer Act and Section 75 of the Public Health Service Act) require presolicitation peer review of the project concept before an RFP may be issued. NCI policy requires concept review of all intra- and interagency agreements, and all renewals and recompetitions of existing contracts and extensions of $100,000 or more for a 6-month or longer period. This review is performed by the Scientific Program Leadership (SPL) Committee and BSA (new concepts and recompetitions with a change in scope).

Once a concept is approved and recommended to the Division Director, the Project Officer, consulting with the Contracting Specialist in the NCI Office of Acquisitions (OA), prepares a statement of work and evaluation criteria. The documents are incorporated into a Request for Contract Project Plan, which is the basis for the official RFP. This document then is presented to the division's senior scientific and management staff for review, comment, and approval. A copy of the plan also is forwarded to the DEA to help verify the evaluation criteria and establish a timetable for the procurement process. The final version of the project plan is incorporated into the RFP by the Contracting Officer, in conjunction with the Project Officer. RFPs must be published in the *Commerce Business Daily* and/or the *NIH Guide for Grants and Contracts*. Occasionally, an RFP may receive wider distribution through publication in scientific journals. Proposals are received by the OA and are checked to be sure they fulfill the RFP requirements and conform to Federal regulations.

R&D proposals that are submitted by the private sector in response to an RFP are evaluated for technical merit by *ad hoc* SEP review groups in a manner similar to that used for the peer review of grant applications. The purpose of the technical merit review is to obtain expert advice on the qualifications of the offeror's staff, the merit of the scientific/technical approaches, the sufficiency of staff and institutional experience, and the availability of equipment and facilities. A DEA SRLB staff member serves as the SRO for each contract review committee. The SROs schedule review sessions, send proposals to committee members in advance of the sessions, and supervise the preparation of the contract review summary reports—brief synop-

ses of the review sessions that contain the numerical scores (as required) and reflect the deliberations and considerations of the reviewers.

In arriving at their recommendations, the peer review committee reviews each proposal. The results of its deliberations are documented by the NCI SRO, who makes the committee findings available to the Contracting Officer. At least three reviewers are assigned to report in depth on each contract proposal during the review meeting. Proposals are reviewed for technical merit and rated for conformance to the evaluation criteria published in the RFP. If competitive, they are scored independently by each committee member, based on the weighted review criteria in the RFP. The individual scores are totaled and averaged to produce a technical merit score for each proposal. Concurrently but independently, the OA evaluates proposals for business considerations.

Project Officers are the NCI program staff members who are responsible for developing and supervising the contract projects. They attend review meetings to provide factual information, but are not permitted to make judgmental or evaluative comments. Representatives of the OA must attend the review sessions to provide guidance on policy and regulations. Review is conducted in accordance with Federal conflict-of-interest regulations.

Following the review session, the SRO forwards the minutes containing the scores, ranking, and individual rating sheets to the Contracting Officer of the OA, who then convenes a Source Evaluation Group (SEG). This group usually consists of the Project Officer and other program staff members, who advise the Contracting Officer on the establishment of a competitive range, based on technical merit scores, cost, and other considerations. Occasionally, site visits are determined to be necessary subsequent to completion of the technical review.

The Contracting Officer informs each offeror in the competitive range of the proposal's deficiencies, ambiguities, or other considerations, as identified by the reviewers or members of the SEG. Offerors are given an opportunity to make minor adjustments in their proposals, which then are reviewed by the contracting and program staff, who serve as a Source Selection Group (SSG). The final decision regarding award of a contract rests with the Contracting Officer who arranges for negotiations with the prospective contractor with advice from the SSG. The total contracting cycle requires 9 to 10 months from receipt of proposals to issuance of an award. Exhibit XI portrays the NCI contract review process.

Following award, the NCI Project Officer performs project surveillance, assisted by the OA. The OA is responsible for debriefing competitors.

NATIONAL CANCER ADVISORY BOARD REVIEW

NCAB Responsibilities

The National Cancer Advisory Board is responsible for the final review of all grant applications referred to the NCI. The Board recommends to the Director of the NCI approval of meritorious grant applications. The NCAB appraises all grant applications with reference to the needs of the Institute and the priorities of the National Cancer Program.

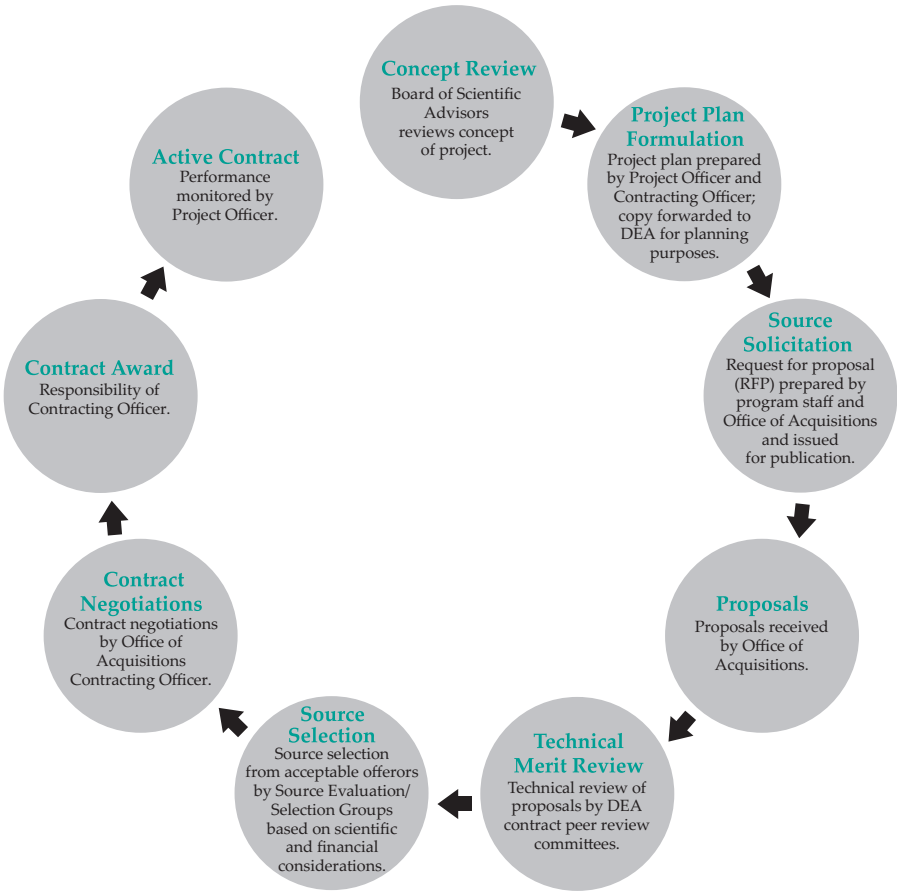
NCAB Meetings

The Board meets at the call of the Director of the NCI or the Chairperson, not less than four times a year. Summary Statements are reviewed three times per year at regularly scheduled meetings. The December NCAB meeting is reserved for the NCI intramural laboratory and extramural program review.

NCAB meetings are open to the public when Summary Statements are not being discussed. Scheduled NCAB meeting dates are published in the *Federal Register* (http://www.gpoaccess.gov/fr/index.html), as required by HHS regulations. Attendance at the closed grant review sessions is limited to Board members, Scientific Review Officers, the NCI Director, appropriate NCI staff, and designated representatives of the Secretary of HHS. A quorum for conducting business will consist of a majority of the currently appointed members.

Approximately 6 to 8 weeks before the NCAB meeting, Summary Statements within the competitive range for applications to be reviewed at the upcoming meeting are made available to all NCAB members via the NIH Electronic Council Book (ECB). This is a restricted access Web site that allows NCAB members to view all of the Summary Statements, as well as the grant applications assigned to them for review based on their areas of scientific interest. (*Note:* NCAB members are not given access to Summary Statements from their own institutions.) By the time the NCAB meets, approximately 3,500 Summary Statements will have been made available

Exhibit XI. NCI Contract Review Process



to the Board members. As described in its Charter, a key role of the NCAB is to "...advise, assist, consult with, and make recommendations to the Secretary, and the Director, National Cancer Institute, ...relating to support of grants and cooperative agreements, following technical and scientific peer review..." This important function is accomplished in the closed session of the NCAB meeting by a committee of the whole known as the Special Actions Subcommittee.

AWARD OF GRANTS

Selection for Funding

Many more grants are approved by the NCAB than can be financed from the NCI budget. Early in the fiscal year, the NCI formulates funding guidelines for its programs based on expected allocations of funds, program requirements, and prior history. Final funding decisions are made by the Director of the NCI and NCI staff, based primarily on IRG percentile/priority score ratings of scientific merit, the Institute's program objectives, avoidance of duplicate effort, and other considerations. The funding mechanisms are reevaluated prior to each grant review cycle and adjusted to the current level of funds available and future funding.

Administrative/Business Review

Following the NCAB grant review session, the NCI conducts an administrative/business review of all applications selected for funding. Applications are reviewed for compliance with NIH policies and for necessary or desirable adjustments in the amounts and terms of the recommended awards.

Notice of Award

The list of applications selected for payment is signed electronically by the NCI Program Director and the Division Director. The signed documents are forwarded to the Extramural Financial Data Branch of the NCI, and the Grants Management Specialist negotiates the award if significant adjustments are required prior to award. The funds then are obligated and recorded in the NIH official accounting records.

For each application selected for payment, a Notice of Award (NoA) is issued by the Grants Management Officer. NoAs are sent solely via e-mail to grantee organizations and are accessible in the eRA Commons. The NoA contains the name and address of the grantee institution and the title of the project. The NoA also names the principal investigator(s) under whose direction the work is to be carried out, the direct and indirect cost awarded, the period of the grant, future years of support, and any special conditions or restrictions under which the grant is awarded.

Congress must be alerted at least 45 hours before the issuance of each new and renewed grant award, so that the appropriate member of Congress may notify his or her constituents. If the award exceeds $1 million, 72 hours' advance notice is required, so that the White House may be informed. This requirement is fulfilled by forwarding a copy of the award notice to the NIH Office of Congressional Liaison at the same time the approval list is signed.

NCI BOARD OF SCIENTIFIC ADVISORS (BSA) CHARTER SUMMARY

AUTHORITY

42 U.S. C. 285a-2(b)(7), section 413(b)(7) of the Public Health Service Act, as amended. The National Cancer Institute Board of Scientific Advisors (Board) is governed by the provisions of the Federal Advisory Committee Act, as amended (5 U.S.C. app), which sets forth standards for the formation and use of advisory committees.

MEMBERSHIP AND DESIGNATION

The Board will consist of 35 members, including the Chair, appointed by the Director, NCI, from authorities knowledgeable in the fields of laboratory, clinical and biometric research, clinical cancer treatment, cancer etiology, and cancer prevention and control, with emphasis on training and experience in the various disciplines and fields related to scientific areas relevant to carcinogenesis, cancer biology and diagnosis, cancer center administration, medicine, radiological and surgical oncology, cancer chemotherapy, cancer epidemiology, cancer prevention and control, cancer education, cancer information services, community outreach, biological, chemical and physical carcinogenesis, DNA repair and effects, tumor biology and immunology, humoral and cellular immunity, hematopoiesis, cell differentiation and transformation, oncogenes and growth factors, molecular and structural biology and genetic regulation, viral oncology, vaccine development, transplantation, chemotherapy, clinical trial design, management and evaluation, pharmacology, drug development and developmental therapeutics, genetic and immunotherapies, pathology, diagnostic research and cytogenetics, biological response modifiers, imaging, nutrition, survey research, epidemiology, biostatistics, rehabilitation, psychology and behavioral medicine, public health and community oncology, quality of life, pain management, cancer detection and diagnosis, cancer treatment and restorative care, dentistry, nursing, public health, nutrition, education of health professionals, medical oncology, surgery, radiotherapy, gynecologic oncology, pediatric oncology, pathology, and biostatistics. All non-Federal members serve as Special Government Employees. Members and the Chair will be invited to serve for overlapping 5-year terms. A member may serve after the expiration of that member's term until a successor has taken office. A quorum for the conduct of business by the full Board will consist of a majority of currently appointed members.

OBJECTIVES AND SCOPE OF ACTIVITIES

The Board will provide advice to the Director and Deputy Director, National Cancer Institute (NCI), and the Director of each NCI Division on a wide variety of matters concerning scientific program policy, and progress and future direction of extramural research programs.

DESCRIPTION OF DUTIES

The Board makes recommendations on research priorities conducted or supported by the Institute. This includes the evaluation of NCI awarded grants, cooperative agreements and contracts and concept review of those activities which it considers meritorious and consistent with the Institute's programs. The advisory role of the Board is scientific and does not include deliberation on matters of public policy.

ESTIMATED NUMBER AND FREQUENCY OF MEETINGS

Meetings of the full Board will be held approximately 3 times within a fiscal year. Meetings will be open to the public except as determined otherwise by the Secretary of Health and Human Services (Secretary) in accordance with subsection (c) of section 552b of Title 5 U.S. C. Notice of all meetings will be given to the public. In the event a portion of a meeting is closed to the public, as determined by the Secretary, in accordance with the Government in the Sunshine Act (5 U.S. C. 552b(c)) and the Federal Advisory Committee Act, a report will be prepared which will contain, as a minimum, a list of members and their business addresses, the Board's functions, dates and places of meetings, and a summary of the Board's activities and recommendations made during the fiscal year. A copy of the report will be provided to the Department Committee Management Officer.

BSA SUBCOMMITTEES

To expedite the BSA's work, *ad hoc* subcommittees may be established to provide additional advice and oversight on specific topics or initiatives. For example, The Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments (TARGET) *ad hoc* subcommittee provides direction of management on an initiative to support the identification and validation of new therapeutic targets to improve the outcome for childhood cancers.

PRINCIPLES OF SELECTION OF AWARD MECHANISMS IN EXTRAMURAL PROGRAMS

DEFINITION OF NEED

Through processes such as program oversight, portfolio analysis, strategic planning, scientific workshops, and occasionally Congressional mandates, scientific opportunities and/or unmet needs are defined which can best be addressed through extramural awards. The choice of award mechanism is dictated by an analysis of the purpose, scope and objective of the research, along with consideration of a number of temporal, regulatory and fiscal parameters.

GRANTS, CONTRACTS, AND COOPERATIVE AGREEMENTS

The decision making process in selection of an award mechanism to achieve an extramural objective requires definition of several fundamental needs and interests of the Government:

Choices to be considered include:

1. Assistance vs. acquisition and procurement.
2. Specific set aside of funds vs. general encouragement of a field. Are market incentives needed?
3. Active vs. passive participation of Government staff.
4. Urgency and one time only vs. extended need and competition.
5. Pool of eligible applicants.
6. Extent of existing capabilities in extramural community.
7. Availability of models and resources and duration of project.
8. Locus of review.

POLICY

The NIH awarding units apply the following criteria for selecting contract, cooperative agreement, and grant instruments to establish appropriate relationships between the NIH and performer organizations for the conduct of extramural R & D activities:

I. Assistance – Grant or Cooperative Agreement

Assistance mechanisms are appropriate when the NIH intends primarily to stimulate, support, or assist a particular research development, training, or related program activity conducted by a recipient under specific legislation authorizing such assistance. Under assistance mechanisms, the NIH identifies general or specific program areas for support, and the performers define and implement the specific aims, objectives, and approaches for their awarded project activities.

A. **Grants** are appropriate when NIH staff has no substantial programmatic involvement with the recipients during performance of the assistance activities.

B. **Cooperative agreements** are appropriate assistance instruments when NIH staff has substantial programmatic involvement with the recipients during performance of the activities.

II. Acquisition – Contracts

Contracts (also Master Agreements and Broad Area Announcements) shall be used for all acquisition, i.e., when the NIH intends primarily to obtain goods, services, research studies, surveys, systems, or property for the direct benefit or use of the NIH or other Government agencies; these agencies may, in turn, provide the end products or results to non-Government parties, including the general public. When acquisition is indicated, the NIH may define specific problems or objectives in a Request for Proposals (RFP), asking offerors to submit their creative or innovative approaches to the contemplated activities. The NIH may specify both the nature of and desired approaches to performing the activities, with the RFP then requesting offerors to describe their capabilities to accomplish the stated requirements.

A. **Master Agreements** – are a form of acquisition where the Government prequalifies a group of offerors with the requisite expertise and resources to perform stated types of research activities, and then may without further review select from the pre-qualified group awardees to conduct the pre-approved activities.

B. **Broad Agency Announcements** – In some circumstances, in order to realize the maximum competition possible pursuant to the Competition in Contracting Act of 1984, and to fulfill requirements for scientific study and experimentation directed toward advancing

the state of the art, or increasing knowledge and/or understanding, the NIH will issue the Broad Agency Announcements.

OPEN AND CLOSED MEETINGS

- Concept review meetings are generally open to the public. Persons who attend or participate in meetings will be eligible to receive contract awards resulting from subsequent RFPs, unless other factors contravene.

- What happens if Concept Review occurs in Closed Session or gets too specific?

Sessions that review specific details of projects or RFPs, will be closed to the public, under authority of 45 CFR 11.5(a) (6) (ii) (c), to protect the free exchange of advisory group members' opinions and avoid undue interference with NIH operations. In those situations, participating reviewers and attendees shall be notified in advance, that, under 42 CFR 52h.5(b) (3), dealing with conflict of interest, they, their close relatives and professional associates, and their organizations, will be ineligible to receive awards resulting from subsequent RFPs, and that the Procurement Integrity Act requirements will apply.

References:

NIH Manual Chapter 1820 – *Selection of Extramural Award Instrument – Grant, Cooperative Agreement, or Contract* (Release date 2/22/85)

NIH Manual Chapter 54513 – *Management and Procedures of National Advisory Councils and Boards in Their Review of Extramural Activities* (Release date 5/15/95)

BOARD OF SCIENTIFIC ADVISORS CONCEPT REVIEW

INTRODUCTION

The National Cancer Institute (NCI) supports both investigator-initiated research and large, directed interdisciplinary and multidisciplinary programs as a comprehensive strategy to unravel the components and complexities of multiple risk factors for cancer, understand specific types of cancer based on their molecular characteristics, and develop rationally designed interventions to prevent, detect, diagnose, and treat cancer and to predict patient response to therapy. The issuance of Funding Opportunity Announcements (FOA) as Requests for Applications (RFA) is an important method for rapidly expanding new research areas that have been identified as high priority areas for the NCI or to implement new initiatives identified in the NCI Strategic Plan and Bypass Budget (http://obf.cancer.gov/financial/plan.htm).

A Request for Applications (RFA) is defined as a formal statement that invites grant or cooperative agreement applications in a well-defined scientific area to accomplish specific program objectives. The RFA indicates the estimated amount of funds set aside for the competition, and submitted applications usually are reviewed by the Institute that issued the RFA. The development and issuance of RFAs is required for a number of research activities, such as cooperative agreements, etc. For example, scientific initiatives requiring the development of large infrastructures or multidisciplinary teams to address complex research questions and translate basic discoveries into the clinic often need coordination and access to additional resources that is best accomplished through cooperative agreements.

Contracts or Requests for Proposals (RFPs) are used when the principal purpose of the transaction is the acquisition of property or services to support NCI-directed research activities. Funds are set aside for these institute-initiated research activities. RFP concepts for research and development (R & D) contracts must be reviewed and approved by the NCI Scientific Program Leadership (SPL) Committee before formal concept review by the extramural Board of Scientific Advisors (BSA). The NCI maximizes opportunities to support investigator-initiated research. To that end, the NCI uses contracts and master agreements for projects that procure research and supporting services to fulfill program objectives and are justified by a strong scientific rationale and NCI research priority.

As scientific opportunities are identified, it is critically important that the development, scientific review, and approval of RFA and RFP concepts be coordinated with budgetary planning. Furthermore, to implement new initiatives, the resources for new and/or expanded activities will have to come from discontinuing support for specific ongoing activities that either have achieved their goals or are no longer high programmatic priorities. Therefore, the NCI must have a very thorough and stringent process for reviewing and approving all initiatives. The NCI process for the development, approval, and issuance of RFAs is described below.

CONCEPT CLEARANCE

A concept is an early planning stage in the development of a research initiative such as a Request for Application (RFA) or a Request for Proposal (RFP). Concept clearance includes review and approval by the NCI Executive Committee and Director followed by BSA review. Each IC must document the clearance of RFA concepts, i.e., purpose, scope, and objectives. 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. One of the primary responsibilities of the BSA is the review and evaluation of concepts for RFAs and RFPs. If a concept is developed into an official initiative, it will be published in the *NIH Guide for Grants and Contracts*.

New Concepts

As scientific opportunities are identified through NCI workshops, meetings, etc., program officials discuss new concepts with their Division/Office/Center (DOC) for further consideration and priority ranking. Multidisciplinary initiatives may require collaborations across DOCs to ensure appropriate scientific oversight and guidance. The following points are considered in the development of new concepts.

- The selection of the appropriate funding instrument (i.e., grant, cooperative agreement, contract) should be carefully considered including whether substantial programmatic involvement is needed to coordinate or facilitate the research effort.
- Program staff should consider whether a Program Announcement on the new scientific opportunity is sufficient to provide additional support.
- Other sources of funding should be explored as part of the RFA or RFP concept development process including co-sponsorship by other NIH Institutes and Centers (ICs), foundations, and private industry.

For approval of co-sponsorship for RFAs initiated by other ICs, the SPL and the NCI Director may approve commitments of $2 million or less total costs per year. SPL and BSA approval is required for all commitments above $2 million total costs in any given year.

Reissued Concepts

The reissuance of an RFA, including multidisciplinary teams and large infrastructures, is dependent on a thorough evaluation of their accomplishments and continued need based upon evaluation plans included in the original RFA Concept.

- Program staff should conduct an evaluation to ensure that the evaluation criteria and milestones set forth in the original concept and RFA document have been met. The evaluation will be an integral component of the consideration of the requested reissuance.

- For a large-scale infrastructure grant or cooperative agreement (e.g., Early Detection Research Network, etc.), an independent panel consisting of NCI and NIH staff members, NIH staff members, and/or extramural investigators should conduct a formal evaluation. The review panel should be asked to provide an assessment of both the accomplishment of the funded investigators and where appropriate (e.g. cooperative agreements) of the NCI staff associated with the initiative. If the DOC Director chooses to support reissuance, the report should be made available to the SPL and subsequently to the BSA. A scientific presentation and overview of the accomplishments of the grant or cooperative agreement is normally scheduled at the BSA meeting prior to the RFA reissuance review.

R&D support contract renewals or RFPs for extramural programs that do not have a **major change** in work scope are not required to undergo BSA review. The SPL reviews contract renewals and determines whether BSA review is needed.

SPL & BSA Concept Approval Process

A Concept Review calendar coordinates SPL evaluation, budget planning, and presentation to the BSA three times per year. The approval process consists of review and approval by:
- NCI Division/Office/Center Director;
- Clinical Trials Operations Committee (clinical trials only);
- Scientific Program Leadership Committee; and
- Board of Scientific Advisors.

BSA RESPONSIBILITIES

The Board shall advise the Director, NCI, and the Director of each NCI Division/Office/Center on a wide variety of matters concerning scientific program policy, and progress and future direction of extramural research programs of each of the Divisions. The BSA's responsibilities include the evaluation of NCI awarded grants, cooperative agreements, and contracts and concept review of those activities which it considers meritorious and consistent with the Institute's programs. The advisory role of the Board is scientific and does not include deliberation on matters of public policy.

• Concept Approval Process

The NCI BSA is charged with approving all RFAs prior to issuance. These presentations are scheduled by the BSA Executive Secretary three times each year (http://deainfo.nci.nih.gov/advisory/bsa/bsa.htm). After SPL approval, the final Request for Concept Approval Form and Concept Justification (see Appendixes K and L) will be submitted electronically for distribution to the BSA members. In addition, the BSA Executive Secretary provides BSA members with the guidelines entitled "NCI Criteria for Use of RFA/RFP Mechanism."

New Concept: The BSA Executive Secretary, in consultation with the BSA Chair, will select BSA members to serve as the primary reviewers for each concept. The BSA Executive Secretary will provide program staff with the names of the assigned reviewers. It is the responsibility of program staff to contact assigned reviewers and respond to any questions prior to the BSA presentation.

Reissuance: In addition to the Concept Approval Form and Concept Justification, the NCI Division/Office/Center Director must prepare a Justification Memo in support of the pending re-issuance. The Justification Memo is attached to the concept documentation and sent to the BSA members. A BSA subcommittee (selected by the BSA Executive Secretary and the BSA Chair) will be assigned to serve as the primary reviewers and determine whether a full presentation to the BSA is needed at a teleconference scheduled by the Executive Secretary. The Justification Memo is an important document in assisting the BSA subcommittee in making these determinations. The BSA subcommittee may request more detailed information from the NCI staff for educational purposes. Subcommittee decision options include: concur with reissuance with no BSA presentation required; concur with reissuance with full presentation to the BSA; or do not concur with reissuance with full BSA presentation. Reviewer comments will be provided to program staff and NCI Division/Office/Center Directors by the BSA Executive Secretary so they may contact the reviewers prior to the meeting as well as include a response in the BSA concept presentation.

• RFA Concept Review Criteria

The following criteria are intended to help NCI staff, the SPL, and the BSA to determine whether proposed RFAs are well justified. Please address these points in preparing your justification.

1. Background:

New concept:

a. Describe the new scientific opportunity and why it should be considered a high priority for the NCI.
b. Indicate how it was identified for additional support (i.e., Congressional legislation, staff and/or scientific working group, etc.).

Reissuance:

a. Describe the continuing scientific need and/or research area that requires reissuance of the RFA.
b. Describe the specific accomplishments of this activity that have contributed to progress in the field.

2. ***Purpose of the RFA:*** In the context of the current state of scientific knowledge in this area, what is the RFA intended to achieve? (Note that the potential impact should be not only scientifically significant, but wide-ranging and clearly more than one might achieve without this initiative.)

3. ***Current Portfolio Analysis:*** Briefly describe current NCI/NIH grant and cooperative agreement/application portfolio (and other related projects) for the research area, specifically addressing: a) funded (active) grants, contracts, and cooperative agreements; b) pending (scored) but unfunded grants; c) applications not scored; and d) any related research funded by other NIH Institutes and/or Centers (ICs). Include the current and one previous fiscal year in the analysis.

4. ***Justification for Use of RFA Mechanism:*** Indicate why an RFA, and not another mechanism (e.g., Program Announcement, contract), is needed to foster and support the research area. Issues to be considered include:

a. need to STIMULATE SUBMISSION of additional applications in a high priority research area (discuss the quality of pending applications and indicate why the stimulation of additional submissions by an RFA will increase the scientific quality of applications or will be more relevant to meeting this scientific opportunity than spontaneously submitted applications);
b. need for INCREASED FUNDING (set-aside funds or exceptions) to encourage submission of applications;
c. need for SPECIAL REVIEW CRITERIA for peer review (indicate why special criteria are needed);
d. need for SPECIAL REVIEW GROUP to review complex area (indicate why no existing CSR study section is adequate to the task); and
e. need to create a NEW ORGANIZATIONAL STRUCTURE that cannot be adequately supported by investigator-initiated mechanisms that don't require a set aside. (Indicate why.)

5. ***Justification of Use of Cooperative Agreement (if applicable):*** For Cooperative Agreements, address the need for STAFF INVOLVEMENT that cannot be met by use of specific terms of award of R01s. What is the expected specific value added of involvement of NCI staff in the project? Discuss why the contract mechanism or traditional investigator-initiated mechanisms are not appropriate based on the level of staff involvement.

For reissuance, describe interactions of staff members with awardees during previous funding period and address the need for continuing staff involvement. For **"limited competition" RFAs**, provide justification for the restriction of eligibility to previous awardees.

6. *Budget:* Give the rationale for the requested level of funding and the number of grants to be supported. All budget estimates should include total costs (direct plus F&A) for each year of support.

7. *Evaluation:*

New concept:

a. Provide a description of the evaluation criteria and metrics (as appropriate) that will be used to evaluate the accomplishments of the RFA initiative.
b. Provide examples of anticipated goals or milestones that would be used to evaluate progress.

Reissuance:

a. Provide the evaluation criteria established and approved in the original RFA Concept. Address whether the anticipated/expected outcomes, goals, and/or milestones were met by the RFA.
b. Describe the specific accomplishments of this activity that have contributed to progress in the field, including clinical advances and/or advances with potential for clinical translation. Cite publications, inventions, patents, and/or collaborations.
c. Was the initiative successful in increasing research funding to this area/field and/or fostering increased research efforts in the targeted area and/or achieving scientific advances?
d. Could the investigators continue the research activities supported by the RFA through other investigator-initiated mechanisms? Should other mechanisms be considered for future support?

For reissuance supporting large infrastructures:

a. An independent panel consisting of NCI staff members, NIH staff members, and/or extramural investigators should conduct an evaluation of large-scale infrastructure grants or cooperative agreements (e.g., Early Detection Research Network, etc.). The evaluation panel members should not be involved directly or receive support from awards resulting from the previous RFA issuance, but they should have sufficient familiarity with the research area to be able to assess the success of the activity.
b. The review should address the criteria outlined in the original Concept including the accomplishment of milestones. The review panel should be asked to provide an assessment of both the accomplishments of the funded investigators and where appropriate (e.g., cooperative agreements), of the NCI staff associated with the initiative.
c. The review panel should provide comments, suggestions, and/or recommendations regarding the continued support, phase out, or transition to other support or investigator-initiated grant mechanisms of the various components supported by the initiative.

R&D Contract Concept Review Criteria

The following review criteria should be applied to Request for Proposal concepts. Appendix K provides a sample form and justification for RFP concepts.

1. *Background:*

a. Describe the NCI organization level that this activity will support.
b. What is the scientific rationale and research priority for this initiative? How was it identified? What constituencies support it/will benefit from it?
c. Identify current related activities, and indicate how this initiative will complement or augment any ongoing activities.

2. *Preliminary Data/Progress to Date:*

For new concepts, indicate any preliminary data supporting the need for and feasibility of additional efforts in this area.

For recompetitions:

a. Provide specific examples of significant contributions to the field that have resulted from the existing contract or master agreement activity. Provide evaluation of success in accomplishing RFP tasks. Include citations of publications, inventions and patents resulting from this activity.
b. Justify with appropriate metrics whether the results were or will be obtained, and if an acquisition/contract remains the appropriate mechanism for conducting such work.

3. *Objectives/Scope:*

For all concepts, indicate the planned objectives and scope of the project, and the intended outcomes. *For recompetitions*, also indicate how these objectives have changed, if at all, based on previous progress and other new information in the field. Discuss these objectives in the context of the NCI mission and the current state of knowledge in the field.

4. *Methods:*

Discuss the adequacy of the methodology to be used in carrying out the activity (*Federal Register Notice* 1/05/2004 52h.11).

5. ***Budget:***
Give rationale for the requested level of funding. For recompetitions, provide funding history of the RFP, including level of support over entire budget period, including modifications to the contract. (e.g., funding actions, exercise of options, changes, supplements, etc.) and the amount of any remaining funding increments and/or capacity currently in the contract to cover the remaining performance period and closeout activities.

6. ***Contract/Master Agreement Justification:***
Indicate why a contract or master agreement is appropriate relative to other mechanisms such as grants and cooperative agreements to accomplish the stated goals. Is the nature of the work for the direct benefit of the government? *For master agreement*, justify the need for this type of mechanism as opposed to contracts. (Give specific reasons.)

BSA DISCUSSION AND APPROVAL

RFA Concept:
In addressing the above issues, consider the actual need for set-asides and special reviews. *The following questions are presented to stimulate thought.*

- If exception funding were to be made available, would a Program Announcement (PA) with multiple receipt/submission dates be more effective?
- If review were conducted by a special review group (CSR or NCI), would a PA be effective (e.g., no set aside)?
- Is there a need for a one time submission date (e.g., to coordinate review and funding of a group of applications)?
- Would an ongoing announcement with multiple receipt/submission dates indicate a continuing NCI interest and allow for better preparation of applications?

RFP Concept:

- Is there a significant need for direction by NCI staff?
- Is there a need for a new organizational structure that cannot be adequately organized or supported by other mechanisms?

Decision Options for New Concept:

- Approval. BSA may suggest a modification in the set aside or change in the RFA mechanism.
- Disapproval.
- Deferral for additional information or modifications. Concept may be presented again at a future BSA meeting. Option to establish subcommittee to work with staff.

Decision Options for Reissuance:
A BSA subcommittee reviews reissuances by teleconference prior to the BSA meeting where a final decision and vote occur. Subcommittee decision options include: concur with reissuance with no BSA presentation required; concur with reissuance with full presentation to the BSA; or do not concur with reissuance with full BSA presentation.

Decision options by BSA include:

- Concurrence.
- Non-concurrence.
- Deferral for additional information or modifications. Concept may be presented again at a future BSA meeting. Option to establish subcommittee to work with staff.

BSA ANNUAL RFA AND RFP CONCEPT REPORT

The annual report on RFA concepts will be provided to the BSA at the November meeting. The report includes a summary of all approved concepts reported by the date the concept was presented to the Board and by the Division in which the concept originated. Also included in the report are:

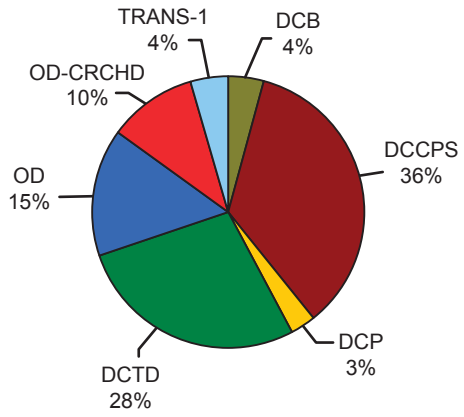
1. RFA grant funding and overall NCI grant funding
2. BSA-approved RFA concept set-asides by Division
3. RFA allocation by concept area
4. NCI grant and RFA funding by concept area as a percentage of total NCI grants
5. Listing of funded grants
6. Abstracts of select funded grants also available in hardcopy and CD-ROM formats

As an example, Exhibit XII illustrates the percentage of the BSA approved RFA set aside for each NCI Division/Office from 2006 through 2009.

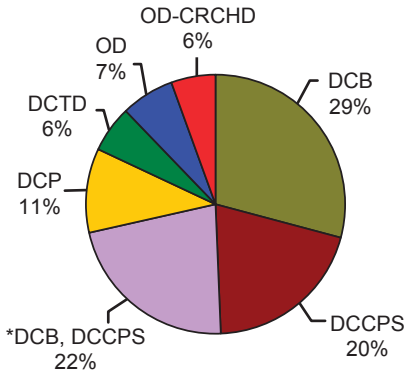
The report has been generated annually since the initial BSA request in 1999, to provide background information relevant to the concept review role played by the BSA. A hardcopy and CD of the *BSA Concept Review Report* is provided to the BSA.

Exhibit XII. BSA Approved RFA Concept Set-Asides by Division/Office/Center

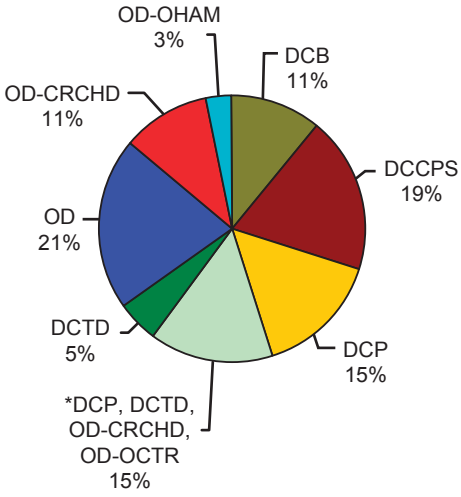
FY2007



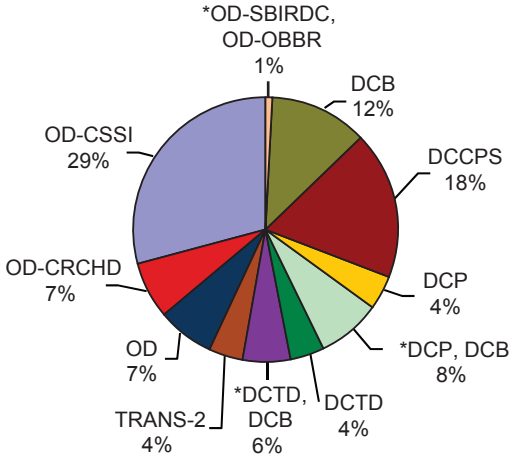
FY2008



FY2009



FY2010



Legend:

DCB	Division of Cancer Biology
DCCPS	Division of Cancer Control and Population Sciences
DCP	Division of Cancer Prevention
DCTD	Division of Cancer Treatment and Diagnosis
OD	Office of the Director
OD-OCTR	Office of the Director - Office of Centers, Training, and Resources
OD-CRCHD	Office of the Director - Center to Reduce Cancer Heath Disparities
OD-OHAM	Office of the Director - Office of HIV and AIDS Malignancy
OD-CSSI	Office of the Director - Center for Strategic Scientific Initiatives
OD-OBBR	Office of the Director - Office of Biorepositories and Biospecimen Research
OD-SBIRDC	Office of the Director - Small Business Innovation Research Development Center
TRANS-1	NCI (DCCPS), Trans-NIH
TRANS-2	NCI (DCTD), Trans-NIH

* Indicates co-funding among NCI Divisions/Offices/Centers.

BSA NCI LISTENS FREQUENTLY ASKED QUESTIONS AND ANSWERS

INTRODUCTION

The BSA has sponsored "NCI Listens" sessions at national scientific meetings to encourage communication with NCI senior staff and BSA members. After a brief presentation highlighting current NCI priorities and activities including new initiatives, attendees ask questions concerning the grant process and comment on other application and funding issues. The questions and answers below are based on the most frequently asked questions from the research community attending NCI Listens sessions from 1997 to 2007.

GENERAL APPLICATION AND SUBMISSION

Where can I find general information on the NIH grants process?

Everything You Wanted to Know About the NCI Grants Process describes how a grant is awarded and administered (http://www3.cancer.gov/admin/gab/2005GPB/GPB05-LowRes.pdf).

The **NIH Office of Extramural Research** provides information on Grant Application Basics and the **Grants Process Overview** (http://grants.nih.gov/grants/grant_basics.htm and http://grants.nih.gov/grants/grants_process.htm, respectively).

NCI Extramural Funding Opportunities provides links to funding initiatives, applications, grant policies, and research resources (http://deainfo.nci.nih.gov/funding.htm).

Where do I find information on the electronic grant application process?

Go to the NIH Office of Extramural Research Web page on the Electronic Application Process for information on how find a Funding Opportunity Announcement (FOA) (http://grants.nih.gov/grants/Electronicreceipt/esub_grantsgov_overview.htm and http://deainfo.nci.nih.gov/faqs-glossary.htm, respectively) and download an application. Information is also provided about the preparation and submission of electronic applications.

Are there mechanisms to support pilot projects?

Yes. The small grant program (R03) and the exploratory/developmental program (R21) (http://grants.nih.gov/grants/funding/r03.htm and http://grants.nih.gov/grants/funding/r21.htm, respectively) both support pilot or feasibility studies that can be carried out in a short time (2 years or less) with limited resources.

The R03 grant mechanism supports different types of projects including pilot and feasibility studies; secondary analysis of existing data; small, self-contained research projects; and development of research methodology. Although the NCI does not accept applications from the NIH R03 Parent announcement, a list of active R03 FOAs published by the NCI can be found on the R03 Web page (http://deais.nci.nih.gov/Public/RFA-PA.jsp?mech=R03).

The R21 mechanism is intended to encourage new, exploratory and developmental research projects by providing support for the early stages of their development. Although the NCI does not accept applications from the NIH R21 Parent announcement, a list of active R21 FOAs published by the NCI can be found on the R01/R21 Web page (http://deais.nci.nih.gov/Public/RFA-PA.jsp?mech=R01,R21).

Does the NCI support international research?

Yes. The NCI Office of International Affairs (OIA) (http://oia.cancer.gov/) coordinates the Institute's worldwide activities, including coordination of cancer research initiatives under agreements between the United States and other countries; planning and implementation of international scientist exchange programs; and sponsorship of international workshops. Go to International Funding Opportunities for additional information (http://oia.cancer.gov/Programs/Pages/programs-funding.aspx).

Foreign institutions and international organizations are also eligible to apply for research project grants, with the exception of Kirschstein-NRSA institutional research training grants, program project grants, center grants, resource grants, SBIR/STTR grants, or construction grants. Information on the grants process specific to foreign applicants is located on Foreign Grant Information.

Go to the Fogarty International Center for information on trans-NIH international programs and training opportunities (http://www.fic.nih.gov/programs/training_grants/index.htm).

How does an investigator state their interest in a dual assignment or cofunding in their grant application?

If your research proposal is relevant to more than one institute, you may request a primary assignment and one

or more secondary assignments in your cover letter. To ensure your research is appropriate for assignment to the NCI, contact the appropriate NCI program director prior to submission.

Dual assignment, or assignment to more than one institute, helps boost your funding chances by providing a backup. If the primary institute doesn't fund it, the secondary institute might or express interest in cofunding.

Are there special paylines for new investigators and early stage investigators?

Yes. The NCI establishes a special payline for new investigators and early stage investigators (ESIs) that is normally 5 percentile points above the R01 payline. Examples of special paylines for new investigators set by NIH institutes are available on the NIH New Investigators Program Web site (http://grants.nih.gov/grants/new_investigators/index.htm). Go to the NCI Funding Policy Web page for information on the current NCI funding policies (http://deainfo.nci.nih.gov/grantspolicies/FinalFundLtr.pdf).

In addition, new investigators and ESIs are more likely to be funded through "exception funding" as a new investigator. Contact the program director listed on your summary statement for more information.

What can the NCI do to support integrated and cross-disciplinary research?

Electronic applications allow more than one Principal Investigator (PI) (on individual research awards (http://grants.nih.gov/grants/multi_pi/). This presents a new and important opportunity for investigators seeking support for projects or activities that require a "team science" approach. Paper applications also may use multiple PIs when the funding opportunity announcement specifically allows them.

The NCI supports program project grants and specialized centers focused on specific research areas that fund integrated and cross-disciplinary research. For examples, see the Specialized Programs for Research Excellence (SPORE) (http://trp.cancer.gov/), Integrative Cancer Biology Program (http://icbp.nci.nih.gov/), and the Centers of Excellence in Cancer Communication Research (http://cancercontrol.cancer.gov/hcirb/CECCRfactsheet.pdf).

The NIH Common Fund (http://commonfund.nih.gov/) provides the opportunity for major initiatives to address gaps in biomedical research that no single institute at the NIH could tackle alone. Many of the new initiatives support integrated and crossdisciplinary research.

Is the NCI working on bioinformatics and methods to share data including data standards?

Yes. The NCI Center for Bioinformatics and Information Technology (CBIIT) (http://ncicb.nci.nih.gov/) leads the effort to provide tools and resources that enable information to be shared along the continuum from the scientific bench to the clinic. For example, one of the goals of the cancer Biomedical Informatics Grid (caBIG) (https://cabig.nci.nih.gov/) is to develop new enabling tools and software systems to collect, analyze, and share data.

The Cancer Therapy Evaluation Program has led the effort to provide tools for participation in clinical trials, including the Clinical Data Update System (CDUS) (http://ctep.info.nih.gov/protocolDevelopment/electronic_applications/cdus.htm) and the Adverse Event Expedited Reporting System (AdEERS) (http://ctep.info.nih.gov/protocol_Development/electronic_applications/adeers.htm).

The Office of Biorepositories and Biospecimen Research (http://biospecimens.cancer.gov/default.asp) has released the NCI Best Practices for Biospecimen Resources (http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf), which provides guiding principles for the collection of biospecimens and related patient data.

Does the NCI support biomedical engineering and what initiatives are available for interdisciplinary research involving biomedical engineering?

Yes. The NCI Center for Strategic Scientific Initiatives (http://cssi.cancer.gov/) coordinates the NCI technology-driven initiatives in the areas of nanotechnology, proteomics, and cancer genomics. The Physical Sciences in Oncology initiative partners scientists in various non-biology disciplines with cancer biology. The Innovative Molecular Analysis Technologies Program (http://innovation.cancer.gov/) supports initiatives on the development of novel technologies suitable for the molecular analysis of cancer, including biomedical engineering approaches.

For training, the Mentored Quantitative Research Career Development Award (K25) (http://www.cancer.gov/researchandfunding/training/K25) supports investigators, with quantitative scientific and engineering backgrounds outside of biology or medicine, who have made a commitment to focus their research on behavioral and biomedical research (basic or clinical).

TRAINING

Where can I find more information about fellowships and training and career awards?

Go to the NCI Training Career Development and Education page (http://www.cancer.gov/researchandfunding/training) or the Diversity Training Branch (DTB), Center to Reduce Cancer Health Disparities (CRCHD) (http://crchd.cancer.gov/diversity/diversity-index.html) for information on training and career development initiatives. To identify the appropriate Program Contact for your area of interest, see the Cancer Training Branch's Program Contact List, the DTB, CRCHD Program Contact List, or contact the program director identified in the Program Announcement.

What does the NCI support for students and investigators from diverse groups, from disadvantaged backgrounds, or with disabilities?

Information on training and career development for individuals from racially and ethnically diverse and medically underserved populations, including eligibility, is available on the CRCHD Training Web site (http://grants.nih.gov/grants/new_investigators/index.htm).

Administrative supplements to existing grants can be provided to investigators who are seeking to support the training of individuals from underrepresented diverse groups, from disadvantaged backgrounds, or with disabilities. For more information, see Research Supplements to Promote Diversity in Health Care Research (http://grants.nih.gov/grants/guide/pa-files/PA-08-190.html).

What opportunities are available for predoctoral fellows to pursue in basic, translational, and clinical careers?

The NCI Ruth L. Kirschstein National Research Service Award (NRSA) for Individual Predoctoral Fellows (F31) (http://www.cancer.gov/researchandfunding/cancer-training/outsidenci/f31) award is to support promising doctoral candidates who will be performing dissertation research and training in scientific health-related fields relevant to the mission of the NCI during the tenure of the award.

The NCI Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Predoctoral MD/PhD Fellows and Other Dual Doctoral Degree Fellows (F30) (http://www.cancer.gov/researchandfunding/cancertraining/outsidenci/f30) award is to support promising predoctoral applicants who have the potential to become productive, independent, highly trained physician-scientists and other clinician-scientists, including patient-oriented researchers in their scientific mission areas. Applicants are encouraged to submit applications during the first 3 years of dual-degree training to ensure that at least 1 year of graduate research training will remain at the time of award.

What opportunities are available for oncology fellows to pursue in basic or translational careers?

The Ruth L. Kirschstein Individual National Research Service Award (NRSA) (http://www.cancer.gov/researchandfunding/training/F32) uses the F32 grant mechanism to support individuals with a doctoral degree (e.g., M.D., Ph.D., Dr.P.H.) for a 3-year period of supervised research experience to achieve independence. The Ruth L. Kirschstein National Research Service Award Institutional Training Grant for T32 programs is also available (http://www.cancer.gov/researchandfunding/training/T32).

The Mentored Clinical Scientist Development Award (http://www.cancer.gov/researchandfunding/training/K08) and Mentored Clinical Scientist Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the NIH K08 grant mechanism to support individuals with a clinical doctoral degree for an intensive, supervised research career development experience in the fields of basic science, biomedical, behavioral, and/or translational research.

The Pathway to Independence Award (K99/R00) (http://grants1.nih.gov/grants/new_investigators/pathway_independence.htm) assists postdoctoral investigators pursuing a research career in the biomedical sciences in transitioning from a mentored postdoctoral position to a stable independent research position.

The NCI Transition Career Development Award (http://www.cancer.gov/researchandfunding/training/K22) and the NCI Transition Career Development Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the K22 grant mechanism to support protected time for clinicians, or equivalent, who are pursuing careers in basic science or in patient oriented research.

What NCI support mechanisms exist for young investigators in the area of cancer prevention, control, behavioral, and population sciences research?

The NCI Cancer Prevention, Control, Behavioral and Population Sciences Career Development Award (http://www.cancer.gov/researchandfunding/training/K07) uses the developmental component of the K07 grant mechanisms to support career development of postdoctoral candidates or mentored junior faculty who are pursuing careers in cancer prevention, control, behavioral, and population sciences.

The NCI Mentored Career Development Award to Promote Diversity (K01) and the NCI Transition Career Development Award to Promote Diversity (K22) (http://crchd.cancer.gov/diversity/cure-overview.html) support the career development of individuals from racially and ethnically diverse and medically underserved populations in the fields of cancer biology, etiology, pathogenesis, prevention, diagnosis, and/or treatment.

The NCI Transition Career Development Award (http://www.cancer.gov/researchandfunding/training/K22) and the NCI Transition Career Development Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the K22 grant mechanism to support protected time for newly independent investigators (e.g., Ph.D.s, Dr.P.H.s, M.D.s) to develop and receive support for their initial cancer-research programs in the prevention, control, behavioral, and population sciences.

The NIH Established Investigator Award in Cancer Prevention, Control, Behavioral, and Population Sciences Research (http://www.cancer.gov/researchandfunding/training/K05) uses the K05 grant mechanism to provide protected time to established investigators so that they can devote their time to conduct research and to mentor junior investigators.

For specific funding initiatives, go to Division of Cancer Prevention Funding and Grants (http://prevention.cancer.gov/funding/funding-grants) or Division of Cancer Control and Population Sciences Funding Opportunities (http://dccps.nci.nih.gov/funding.html).

What type of support is available to transition from postdoctoral positions to independent investigators?

The NCI Transition Career Development Award (http://www.cancer.gov/researchandfunding/training/K22) and the NCI Transition Career Development Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the K22 grant mechanism to support "protected time" for newly independent investigators to develop and receive support for their initial cancer-research programs. This award is intended to facilitate the transition of investigators from the mentored to the independent stage of their careers. It applies to clinicians (e.g., M.D.s and Doctoral level Oncology Nurses) who are pursuing basic science careers; clinicians who are pursuing careers in patient-oriented research; and individuals (e.g., Ph.D.s, Dr.P.H.s, M.D.s) pursuing careers in the prevention, control, and population sciences.

The Pathway to Independence Award (K99/R00) (http://grants1.nih.gov/grants/new_investigators/pathway_independence.htm) provides up to 5 years of support, divided into two phases. Phase I provides 1 to 2 years of mentored support under a K99 mechanism. Phase II provides up to 3 years of independent research support under an R00 mechanism.

What NCI Career Development Awards exist for physician scientists interested in patient oriented or clinical research?

For the purpose of this question, the term "physician scientists" includes clinicians pursuing careers in laboratory-based basic science as well as patient-oriented research. Additionally, the term "clinical research" is research in which the identity of the patients or the identity of the patients from whom cells or tissues under study are obtained is known. Finally, patient-oriented research is research conducted with human subjects (or on material of human origin) for which an investigator (or colleague) interacts directly with human subjects.

The NIH Mentored Patient-Oriented Research Career Development Award (http://www.cancer.gov/researchandfunding/training/K23) and the NCI Mentored Patient-Oriented Research Career Development Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the K23 grant mechanism to support the career development of clinically trained professionals who have made a commitment to focus on patient-oriented research.

The NIH Mentored Clinical Scientist Development Award (http://www.cancer.gov/researchandfunding/training/K08) and NCI Mentored Clinical Scientist Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the NIH K08 grant mechanism to support individuals with clinical doctoral degrees who have made a commitment to focus on laboratory-based basic science, biomedical, behavioral, and/or translational research.

The NCI Mentored Career Development Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) uses the NIH K01 grant mechanism to support the career development of individuals with a doctoral degree in the fields of cancer biology, etiology, pathogenesis, prevention, diagnosis, and/or treatment. Applicants for this award are limited to individuals from racial and ethnic minority groups; or with disabilities; or from disadvantaged backgrounds.

The NCI Transition Career Development Award (http://www.cancer.gov/researchandfunding/training/K22) and the NCI Transition Career Development Award to Promote Diversity (http://crchd.cancer.gov/diversity/cure-overview.html) use the NIH K22 grant mechanism to support protected time for newly independent physician

scientists who are pursuing basic science or patient oriented research careers to develop their first independent research program.

The NIH Mid-career Award in Patient-Oriented Research (http://www.cancer.gov/researchandfunding/training/K24) uses the NIH K24 grant mechanism to provide mid career clinical investigators with protected time (1) for patient-oriented research and (2) to act as mentors for junior clinical investigators.

The NCI Paul Calabresi Career Development Award For Clinical Oncology (http://grants.nih.gov/grants/guide/pa-files/PAR-06-449.html) uses the K12 grant mechanism to support a research career development experience for medical doctors and basic science researchers in the design, development, and implementation of hypothesis-based therapeutic cancer clinical trials.

Does the NCI provide support for cancer education?

Yes. The NCI Cancer Education and Career Development Program (R25T) (http://www.cancer.gov/researchandfunding/training/R25T) supports the development and implementation of curriculum-dependent programs to train predoctoral and postdoctoral candidates. The NCI Cancer Education Grant Program (R25E) (http://www.cancer.gov/researchandfunding/training/R25E) provides funding for the development of cancer education programs and cancer research dissemination projects that can be completed within 5 years.

Are all training mechanisms restricted to U.S. citizens or visa holders?

Yes, with one exception: the Pathway to Independence Award (K99/R00) (http://grants1.nih.gov/grants/new_investigators/pathway_independence.htm). Otherwise, you must be a U.S. citizen, a noncitizen national, or a permanent resident with a valid Alien Registration Receipt Card (a "green card") (http://deainfo.nci.nih.gov/faqs-glossary.htm) at the time of award.

CLINICAL RESEARCH

Is there a source for information on the preparation of clinical research grant applications?

The Center for Scientific Review (CSR) has developed a Web site for Advice to Investigators Submitting Clinical Research Applications (http://cms.csr.nih.gov/ResourcesforApplicants/AdvicetoInvestigatorsSubmittingClinicalResearchApplications.htm). The Web site also contains links to policies and institute contacts.

See Conducting Clinical Trials (http://www.nci.nih.gov/clinicaltrials/conducting/) for links to NCI clinical trials resources.

What resources and programs are available to assist clinicians in carrying out drug development and clinical research?

The Cancer Therapy Evaluation Program (CTEP) (http://ctep.info.nih.gov/) provides access to a wide variety of resources, including Clinical Investigator forms and electronic applications for the standardization of trial data collection and reporting, including common toxicity criteria and common data elements. The Investigator's Handbook (http://ctep.cancer.gov/investigatorResources/investigators_handbook.htm) provides information on the policies and procedures for participants in clinical trials of investigational agents sponsored by the NCI. The Clinical Trials Support Unit (CTSU) (https://www.ctsu.org/) allows physicians who are not affiliated with a cooperative group to enroll patients on NCI-sponsored clinical trials.

The NCI Experimental Therapeutics (NExT) (http://dtp.nci.nih.gov/index.html) Program supports drug discovery and development projects from preclinical development of an agent with a specific target through proof of concept clinical trials (http://dtp.nci.nih.gov/screening.html). Submission deadlines occur three times per year.

Contact the Division of Cancer Prevention (http://prevention.cancer.gov/clinicaltrials) for information on prevention clinical trials. Contact the Division of Cancer Control and Population Sciences (http://dccps.nci.nih.gov/) for information on behavior, clinical epidemiology and genetics, survivorship, and outcomes research.

The Cancer Biomedical Informatics Grid (caBIG™) (https://cabig.nci.nih.gov/) is developing a comprehensive set of clinical trials management tools including an adverse event reporting module, a clinical trials participant registry, a clinical data exchange system and a patient study calendar.

Visit the NCI Clinical Trials (http://www.cancer.gov/clinicaltrials) Web site for information on NCI-sponsored clinical trials, clinical trial results, and education materials.

How can primary care physicians become involved in primary and secondary prevention studies?

The Community Clinical Oncology Program (CCOP) (http://prevention.cancer.gov/programs-resources/programs/ccop) supports a network linking academic institutions with community medical practitioners for conducting cancer prevention and treatment clinical tri-

als. Primary care physicians are encouraged to become involved with their local CCOP program.

The National Cancer Institute Community Cancer Centers Program (NCCCP) (http://ncccp.cancer.gov/) is designed to encourage the collaboration of private-practice medical, surgical, and radiation oncologists with NCI-supported cancer centers to provide state-of-the-art cancer care and prevention.

Should the NCI support the development of clinical trial management tools that would allow researchers to access and use data to consider individual treatment, new trial designs, etc.?

This issue was addressed in the Clinical Trials Working Group report published in 2005. In response to the report, the Cancer Biomedical Informatics Grid (caBIG™) (https://cabig.nci.nih.gov/) is developing a comprehensive set of modular, interoperable, and standards-based tools designed to meet clinical trials management needs. Examples of these tools include an adverse event reporting module, a clinical trials participant registry, a patient study calendar, and a lab information exchange module and may be viewed at the Clinical Trials Management Systems (CTMS) Workspace (https://cabig.nci.nih.gov/workspaces/CTMS/?pid=primary.2006-10-24.9768040952&sid=ctmsws&status=True). In addition, the Coordinating Center for Clinical Trials (http://ccct.cancer.gov/) is leading the effort to establish a comprehensive database containing information on all NCI-funded clinical trials to facilitate better planning and management across clinical trial venues.

Since physicians are not aware of many clinical trials, are there marketing tools to assist physicians and patients?

The NCI Clinical Trials Web site (http://www.cancer.gov/clinicaltrials/) provides information on clinical trials, trial results, and education materials. The PDQ (Physician Data Query) (http://www.cancer.gov/cancertopics/pdq/cancerdatabase) is NCI's comprehensive cancer database on active clinical trials and includes peer-reviewed summaries. Clinical trials information on all NIH-sponsored clinical trials can be accessed through the Web site (http://clinicaltrials.gov/).

The Cancer Information Service (CIS) educates the public about cancer. Fact Sheets are available at the CIS Web site (http://www.cancer.gov/cancertopics/factsheet/Information/CIS) and cancer information specialists will answer questions at 1-800-4-CANCER. See the NCI Publications Locator (https://cissecure.nci.nih.gov/ncipubs/home.aspx?js=1) to view and order NCI publications.

The Clinical Trial Education Series (CTES) (http://www.cancer.gov/clinicaltrials/learning/clinical-trials-education-series) is a group of 13 different educational materials (booklets, slides, videos) to target education and outreach for health professionals and patients.

The Cancer Biomedical Informatics Grid (caBIG™) (https://cabig.nci.nih.gov/) is developing a comprehensive set of clinical trials management tools including an adverse event reporting module, a clinical trials participant registry, a clinical data exchange system and a patient study calendar.

Are NCI-supported human specimen banks available to investigators?

Yes. The Specimen Resource Locator (http://pluto3.nci.nih.gov/tissue/default.htm) is a database to help researchers locate human specimens (tissue, serum, DNA/RNA, other specimens) for cancer research. It includes tissue banks and tissue procurement systems with access to normal, benign precancerous, and cancerous human tissue from a variety of organs.

In addition, the Office of Biorepositories and Biospecimen Research (OBBR) (http://biospecimens.cancer.gov/default.asp) was established in 2005 to guide, coordinate, and develop the NCI's biospecimen resources and capabilities. OBBR activities include establishment of the Biospecimen Research Network (http://biospecimens.cancer.gov/researchnetwork/default.asp) and the Biospecimen Research Database (https://brd.nci.nih.gov/BRN/brnHome.seam), development of NCI Best Practices for Biospecimen Resources (http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf), and sponsoring a series of Biospeciman Best Practices Forums (http://biospecimens.cancer.gov/practices/forum/).

The Cancer Biomedical Informatics Grid (caBIG™) (https://cabig.nci.nih.gov/) has developed tissue bank repository tools and supports the Shared Biospecimen Data Directory (https://cabig.nci.nih.gov/workspaces/TBPT/biospecimen-data-directory/).

Contact staff in the Office of Biorepositories and Biospecimen Research or Cancer Diagnosis Program for more information.

How do patient advocates participate in NCI's research activities and programs?

The NCI has established the Consumer Advocates in Research and Related Activities (CARRA) program within the Office of Advocacy Relations (OAR). The CARRA program was created to integrate the perspective of people

affected by cancer into a wide range of NCI's programs and activities, including peer review of clinical research. See the CARRA Web page (http://carra.cancer.gov/) for more information.

Is there a nomination process for the Clinical Trials and Translational Research Advisory Committee (CTAC) membership? How is this committee being constituted?

There is not a nomination process. The CTAC includes current members from the major NCI boards/committees and representatives from the appropriate clinical and scientific areas. See the CTAC Web site for meeting schedule, minutes, and membership (http://deainfo.nci.nih.gov/advisory/ctac/ctac.htm).

PEER REVIEW

Where can you find basic information about peer review?

See Grant Application Basics (http://grants.nih.gov/grants/grant_basics.htm) and the Peer Review Process (http://grants.nih.gov/grants/peer_review_process.htm) for information.

The Center for Scientific Review also provides an overview on the Peer Review Process (http://cms.csr.nih.gov/ResourcesforApplicants/PolicyProcedureReview+Guidelines/) including a video of a study section meeting. Guidelines for Reviewers (http://cms.csr.nih.gov/peerreviewmeetings/reviewerguidelines/) provides important information on the review criteria for grant applications including guidelines for human subjects research and specific grant mechanisms.

How do you determine the best study section for your application?

On the NIH Center for Scientific Review (CSR) (http://cms.csr.nih.gov/AboutCSR/Welcome+to+CSR) Web site, go to CSR Study Section Roster Index (http://www.csr.nih.gov/Committees/rosterindex.asp) to find descriptions of the research areas for each study section and the study section membership. This information can help you determine the appropriate study section. In many cases, there may be more than one study section suitable for your grant application. It is highly recommended that you contact your NCI program director (http://www.cancer.gov/researchandfunding/contacts) or the study section Scientific Review Officer (SRO) (http://deainfo.nci.nih.gov/faqs-glossary.htm), who can assist you in determining the best study section. To request a specific study section and institute assignment, include the information in your cover letter (http://deainfo.nci.nih.gov/faqs-glossary.htm).

Is there a way to shorten the review process so that investigators can receive the review outcome and resubmit more rapidly?

Beginning with the September/October 2007 study section meetings, new investigators (http://deainfo.nci.nih.gov/faqs-glossary.htm) now have the option of submitting a resubmission/amended (http://deainfo.nci.nih.gov/faqs-glossary.htm) R01 application for consecutive review cycles, saving 4 months. The summary statements (http://deainfo.nci.nih.gov/faqs-glossary.htm) for qualifying applications will have an explicit note indicating eligibility for next cycle submission. See NOT-OD-07-083 (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-07-083.html) for more information.

How does the NIH ensure that peer review panels have the appropriate expertise and experience and how can I ensure that my application gets an appropriate review?

Peer review is conducted by panels of reviewers with broad expertise. These panels may include some ad hoc review members with expertise in relevant areas of science. However, it is impossible to have experts in each grant application's specific research area on study sections that review up to 120 applications. If you feel the assigned study section does not have the appropriate expertise, contact the Scientific Review Officer (SRO) (http://deainfo.nci.nih.gov/faqs-glossary.htm) to discuss the general areas of expertise needed. You may also include this information in a cover letter (http://deainfo.nci.nih.gov/faqs-glossary.htm).

One of the Enhancing Peer Review at NIH recommendations that have been instituted is the clustering of new investigator and clinical applications in study sections.

What is being done to recruit senior and experienced peer reviewers?

Scientific Review Officers (http://deainfo.nci.nih.gov/faqs-glossary.htm) strive to recruit senior and experienced peer reviewers whenever possible. The majority of reviewers serving on CSR study sections are successful peer reviewed investigators at the Associate Professor level or above. A description of "How Scientists are Selected for Study Section Service" is provided on the CSR Web site. Training committees or ad hoc committees organized to review specific initiatives, such as RFAs (http://deainfo.nci.nih.gov/faqs-glossary.htm), may have junior investigators if the scientific area is a narrow research field and many of the senior experts have applied.

The NIH is striving to recruit experienced reviewers and improve reviewer retention by providing reviewers more flexibility regarding their tour of duty, and by instituting a continuous R01 applications submission process for members of standing study sections (NOT-OD-08-026) (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-026.html) and reviewers with recent substantial service (NOT-OD-11-093) (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-11-093.html). See Enhancing Peer Review (http://enhancing-peer-review.nih.gov/engage_the_bestreviewers.html) for more information on recommendations for recruiting the best reviewers.

How can participation in peer review be increased?

To address this problem and others, the NIH Director called upon leaders from across the scientific community and the NIH to join a trans-NIH effort to examine the two-level NIH peer review system with the goal of optimizing its efficiency and effectiveness. Information on their recommendations is available on the NIH Web site, Enhancing Peer Review (http://enhancing-peer-review.nih.gov/). New policies include the expanded use of teleconferences and virtual reviews. Standing study section members are now offered the option of serving a 4-year (three meetings a year) or 6-year (two meetings a year) term. More flexibility is available through the use of virtual reviews for some applications.

In addition, the NIH has implemented an alternate plan for submission and review of research grant applications from appointed members of chartered CSR study sections and reviewers with recent substantial service to recognize their outstanding service and to minimize disincentives to study section service. See NOT-OD-11-093 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-11-093.html) for more information.

Summary statements do not clearly reflect the peer review discussion, and review of resubmissions often focuses on new concerns rather than the previous critique.

In summary statements that are scored, a summary of discussion is included prior to the individual reviewer critiques to reflect the peer review discussion at the study section meeting. For resubmitted (amended) applications, new reviewers in addition to previous reviewers are usually assigned. They are instructed to review whether previous concerns have been addressed as well as comment on any new concerns. Contact your program director (http://deainfo.nci.nih.gov/faqs-glossary.htm) to discuss how to best respond to your summary statement.

There is concern that innovation in research is not adequately emphasized in peer review.

The NIH Common Fund (formerly Roadmap) has created new high risk research programs to encourage innovation, such as the NIH Director's Pioneer Award (http://nihroadmap.nih.gov/pioneer/), NIH Director's New Innovator Award (http://nihroadmap.nih.gov/newinnovator/), and the Transformative R01 Program (http://nihroadmap.nih.gov/T-R01/).

In addition, many of the recommendations of the NIH report on "Enhancing Peer Review at NIH" encourage reviewers to emphasize innovation rather than methodology in their reviews. See the NIH Web site, Enhancing Peer Review (http://enhancing-peer-review.nih.gov/), for more information and a timeline for implementation.

How does the appeals process actually function?

The NIH has a formal process to resolve disagreements between applicants and NIH review committees and/or NIH staff concerning the referral (assignment) and review of applications. Note that disagreements are not necessarily grounds for appeal. The NIH appeals policy and process (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-11-064.html) is described in the *NIH Guide for Grants and Contracts*.

Before beginning the appeals process, the applicant is strongly advised to speak with the NCI program director (http://deainfo.nci.nih.gov/faqs-glossary.htm) responsible for the application. The program director can explain the options and their consequences and is often in a position to help the applicant understand the study section's recommendation. Appeal letters should be submitted to the NCI program director (http://deainfo.nci.nih.gov/faqs-glossary.htm). The NCI will make the appeal letter together with the staff recommendation available to the National Cancer Advisory Board (http://deainfo.nci.nih.gov/advisory/ncab/ncab.htm) for the second level of review.

Can administrative cuts be appealed? Is there a process for restoration of administrative cuts?

Administrative cuts cannot be appealed. If you find that you are unable to perform the research included in your grant application due to substantial administrative cuts, contact your program director (http://deainfo.nci.nih.gov/faqs-glossary.htm). The work scope of your research grant may be renegotiated or an administrative supplement may be considered in unusual circumstances.

BUDGET

What is the NCI Bypass Budget?

Each year, as mandated by the National Cancer Act of 1971 (P.L. 92-218), the NCI prepares the NCI Bypass Budget (http://obf.cancer.gov/financial/plan.htm), which describes continuing and new activities that take advantage of new discoveries and opportunities and maximize the use of NCI resources. This annual plan and budget proposal are provided directly to the President of the United States for formulating the budget request to Congress.

How are funding decisions made?

The NCI no longer publishes RPG paylines. Individual consideration of a broad range of competing applications will be the hallmark of NCI's selection process. Peer review evaluation of scientific merit will remain the primary consideration in these funding decisions, which will be made by NCI Scientific Program Leaders (SPL) following discussions with Program Staff. The NCI SPL will give special consideration to applications that fill a significant gap in the cancer research portfolio or propose an especially novel or promising scientific approach. Although there are no guaranteed paylines, the SPL does identify a percentile cutoff for R01s and R21s, then discusses additional applications for funding above the percentile. The NCI has a strong commitment to new investigators, including early stage investigators, and establishes a higher percentile cutoff for these R01 applications. More information is available at NCI Funding Policy (http://deainfo.nci.nih.gov/grantspolicies/FinalFundLtr.pdf). Funding decisions for Request for Applications (RFA) are determined by the set aside of funds available and the quality of the grant applications.

How are funding decisions made for applications submitted in response to program announcements?

The payline for R01 applications in response to PAs is no different than if they are submitted in response to the parent announcement. However, if the application is close to the payline, it may be eligible for funding by exception. Contact the program director listed on your summary statement for more information on "exception funding."

Where is information available on the funding level in specific disease or research areas?

The NCI reports how appropriated funds are spent in a number of different categories or classifications including specific cancer sites, cancer types, and diseases related to cancer, as well as types of research mechanisms. See the NCI Fact Book (http://obf.cancer.gov/financial/factbook.htm) for information on funding of disease categories as well as funding and success rates for grant mechanisms.

The NCI's Funded Research Portfolio (http://deainfo.nci.nih.gov/AwardSearch.htm) provides access to various NCI budget reports associated with research funding by research categories. It also provides the ability to search the database in various ways including a text search of the project abstract and a search of the NIH research categories that are assigned to the projects by extramural and intramural groups (http://fundedresearch.cancer.gov).

The International Cancer Research Portfolio (http://www.cancerportfolio.org/index.jsp) represents a searchable database of information on cancer research awards of the cancer funding organizations that comprise the International Cancer Research (ICR) Partners (http://www.cancerportfolio.org/index.jsp).

The NIH report, Estimates of Funding for Various Diseases, Conditions and Research Areas (http://report.nih.gov/rcdc/categories/), includes funding levels for grants and contracts across the NIH by fiscal year.

Where can I find information on paylines and funding policies for the NCI?

Information on the current payline for R01 (http://obf.cancer.gov/financial/factbook.htm) applications and funding policies for competing (http://deainfo.nci.nih.gov/faqs-glossary.htm) and non-competing (http://deainfo.nci.nih.gov/faqs-glossary.htm) applications is available on the NCI Funding Policy (http://deainfo.nci.nih.gov/grantspolicies/FinalFundLtr.htm) Web page. Information on NIH grant policies and other policy resources is available on the Grants Policy and Guidance (http://grants.nih.gov/grants/policy/policy.pdf) Web page.

Where is information available on success rates, including new investigator success rates?

See the NCI Fact Book (http://obf.cancer.gov/financial/factbook.htm) for information on funding of disease categories as well as funding and success rates for grant mechanisms. The Research Portfolio Online Reporting Tools (RePORT) web site provides information on NIH success rates (http://report.nih.gov/index.aspx) by institute, grant mechanism, medical school, application type, and other categories.

RePORT also provides information on new investigator (http://deainfo.nci.nih.gov/faqs-glossary.htm) success rates and training and career development success rates (http://acd.od.nih.gov/).

OTHER TOPICS

What products and services from the intramural program and NCI-Frederick are accessible to extramural investigators?

Many NCI resources are available to extramural investigators including screening and production of compounds, animal resources, genomic resources, and scientific computing resources. See NCI Research Resources (http://resresources.nci.nih.gov/) for more information.

What is the NIH Common Fund? How are these initiatives being coordinated and reviewed?

The NIH Common Fund is an effort to transform the Nation's medical research capabilities and speed the movement of research discoveries from the bench to the bedside. The Common Fund supports the series of transformative programs that were established under the NIH Roadmap for Medical Research, as well as other non-Roadmap activities. Programs include the NIH Director's Pioneer awards, New Innovator awards, and Transformative R01 Program. For complete information, visit the Common Fund (http://nihroadmap.nih.gov/) site.

The Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) (http://opasi.nih.gov/) is responsible for managing the process by which trans-NIH initiatives are prioritized for consideration and evaluation by both outside advisors and NIH leadership.

Who is the point of contact for nominations for Boards or review committees?

Contact the Director, Division of Extramural Activities, NCI, if you are interested in volunteering for NCI peer review committees or Boards. For CSR peer review committees, go to "How to Become a CSR Reviewer" (http://cms.csr.nih.gov/PeerReviewMeetings/StudySectionReviewers/ServiceasReviewers.htm) for information on reviewer qualifications and the CSR nomination process.

SUMMARY OF ETHICS RULES FOR SPECIAL GOVERNMENT EMPLOYEES SERVING ON ADVISORY COMMITTEES

INTRODUCTION

As a special Government employee (SGE), you *are* a Federal Government employee. As such, you are covered by the executive branch ethics rules, although in a somewhat less restrictive manner than regular Government employees.

The Criminal Conflict of Interest Statutes 18 U.S.C. §§ 203, 205, 207, 208

Financial Conflicts: You are prohibited from participating personally and substantially in **any particular matter** that directly and predictably affects your own financial interests or the financial interests of certain other persons or organizations: your spouse, minor child, general partner, and outside organizations with which you serve as an officer, director, trustee, or employee, or with which you are negotiating for or have an arrangement for future employment. If your duties would require you to participate in any particular matter that affects your financial interests, you have a conflict of interest which you will have to resolve. Of most concern are reviews of grant proposals or contract applications, or similar funding decisions; recommendations or approvals of scientific studies, projects, clinical trials, and new drug applications; and other actions that involve deliberation, decision, or action affecting the legal rights of identified parties. You might also be prohibited from involvement in **Particular Matters of General Applicability**. For example, recommendations of regulations, policies or standards that affect an industry, group of manufacturers, or health care providers.

Divestiture: Sell or otherwise dispose of the financial interest that is creating the conflict.

Waiver: Get written approval from a senior official to continue with your work for the committee despite the conflict. Waivers can be granted where there is a pressing need for a particular individual's services on the committee and this outweighs the potential for conflict of interest. Specific criteria must be met. This is considered a "general waiver" in that **it only allows participation in matters that affect all institutions, or types of institutions, similarly.**

Concurrent Representation: While you are serving, there are **representational restrictions** on contacting the Government on behalf of another—for example, as an agent or attorney—with intent to influence on a specific party matter that you are working on as an SGE.

Post-Employment Representation: You cannot "switch sides" in the private sector and represent back to the Government concerning the same specific party matter—the same contract or grant, for example, that you worked on as an SGE. (Remember also the restrictions resulting from employment negotiations that are covered by the financial conflict statute.)

Standards of Ethical Conduct 5 CFR Part 2635

You are prohibited from receiving compensation for **teaching, speaking, or writing** about your Government duties or about any topic if the invitation to teach, speak, or write comes from a person substantially affected by the matters on which you work as an SGE. However, you may teach courses about general topics requiring multiple presentations.

You may not accept **gifts** offered as a result of your advisory committee membership. In many circumstances, you may not participate as an **expert witness** on any matter or proceeding that you work on as an SGE.

Impartiality: You are prohibited from participating in a specific party matter where a reasonable person would question your impartiality—for example, conducting a review of a grant application submitted by your mentor or someone with whom you have a close relationship— unless authorized by an agency designee to participate.

Misuse of Position—Use of Public Office for Private Gain: This includes the misuse of nonpublic information, government property, and official time. You may not use your position to imply that the Committee endorses your private activities or refer to your Government position for your own private gain.

Employment by, or Gifts from, Foreign Governments: Committee member may be employed by a foreign government, which includes positions with foreign universities that are government operated. There are also statutory provisions restricting acceptance of gifts including awards, educational scholarships, and travel expenses occurring outside the Unites States, but not on travel or honoraria for speaking engagement or employment for consulting.

Lobbying: In their official capacities or as a group, committee members are prohibited from engaging in any activity which directly or indirectly encourages or directs any person or organization to lobby one or more members of Congress. You may appear for the purpose of informing or educating the public about a particular policy and you may communicate with members of Congress at their request.

Political Activities (Hatch Act): *While on Government duty* (unlike the other rules which always apply during your time of appointment), you may not engage in partisan political activities, run for political office in a partisan election, or solicit contributions from the public. For more information on political activity restrictions, please see the Office of Special Counsel website at www.osc.gov.

Ethics for SGEs: Your Responsibilities as a Government Employee

- Complete the OGE-450 Financial Disclosure Report and submit it for review. You should not attend meetings or participate in committee business until this form is submitted and reviewed.
- Complete the HHS-697 Foreign Activities Questionnaire and submit it for review.
- If conflicts of interest are identified, work with committee managers and ethics officials to resolve them.
- Complete a financial disclosure form 30 days prior to each Board meeting.
- Complete initial ethics orientation and yearly ethics training—you should have a basic knowledge of the Standards of Ethical Conduct and the Conflict of Interest Statutes.
- Monitor changes in your circumstances that might create new conflicts.
- Be sure to contact your Designated Federal Official (DFO) or ethics officials with any questions.

Excerpted from: *Overview of the Ethics Rules for Special Government Employees Serving on an Advisory Committee,* U.S. Office of Government Ethics, NIH (see p. 61)

Financial Conflicts of Interest Office of Government Ethics – OGE 450 Form

Office of Government Ethics (OGE) 450 Form: http://ethics.od.nih.gov/topics/450-info.htm

Financial Interests to be reported on the OGE 450 Form include:

- Stocks, stock options, bonds
- Sector funds (Waiver available for biotech/health care sector funds up to aggregate value of $50,000)
- Earned income including salaries, fees, and/or honoraria
- Limited partnerships and venture capital corporations
- Non-Federal research/training support
- Invention rights and royalties
- Real estate, trades and businesses, and partnership interests
- Speaking engagements and consultant work

SGEs report assets with a fair market value greater than $1,000 at the close of the reporting period, which produced income over $200.

Conflict of Interest and Ethics Web Sites

U.S. Office of Government Ethics

- Online training on Ethics for Special Government Employees: http://www.usoge.gov/Education/Education-Resources-for-Federal-Employees/Ethics-Training-for-Special-Government-Employees-WBT/
- Online training on Completing the OGE Form 450: http://www.usoge.gov/training/module_files/oge450_wbt_06/homepage.html

A Guide on the Ethics Rules That Apply to Advisory Committee Members Serving as Special Government Employees: http://www.usoge.gov/uploadedFiles/Education/Education_Resources-for-Ethics-Officials/Resources/bkServeHonor.pdf

Overview of the Ethics Rules for Special Government Employees Serving on Advisory Committees: http://ofacp.od.nih.gov/ethics/SGE3.pdf

Ethics Rules for Advisory Committee Members and Other Individuals Appointed as Special Government Employees (SGEs): http://ofacp.od.nih.gov/ethics/SGETRAININGOCT2004.pdf

NIH Administrative Fact Sheet for Special Government Employees: http://ofacp.od.nih.gov/ethics/AdminFactSheetforSGEsOct2009.pdf

Foreign Activities:

- U.S. Constitution Emoluments Clause: http://www.csr.nih.gov/roster_proto/nihlist.htm
- Foreign Activities Questionnaire: http://ethics.od.nih.gov/forms/hhs-697.pdf

Conflict of Interest and the Special Government Employee: http://ethics.od.nih.gov/topics/OGE-SGE.pdf

NIH Ethics Program: http://ethics.od.nih.gov/default.htm

Bioethics Resources on the Web: http://bioethics.od.nih.gov/conflict.html

To Serve With Honor

A Guide on the Ethics Rules
That Apply to Advisory Committee
Members Serving as Special
Government Employees

U.S. Office of Government Ethics
www.usoge.gov
March 2008

Contents

To Serve With Honor

A Game Plan for Success

A Guide on the Ethics Rules
That Apply to Advisory Committee
Members Serving as Special
Government Employees

Congratulations on becoming a member of the Government's advisory team! In your new committee position, you may be helping to shape public policy or making other contributions that impact important issues facing our country. Your service on the committee will be a rewarding experience. But, while your membership has it rewards, it also has its ethical obligations. Being a member of the Government's team means you'll have to learn to play by the Government's ethics rules. These ethics rules help promote public confidence and trust in our Government and in the recommendations that your committee will make to the Government. These rules will also help ensure that you serve the Government and your committee honorably.

In this summary, you will learn more about the ethics laws and rules that apply to your service as a member of a Federal advisory committee. We will highlight some of the ethics rules that are most likely to affect you during your Government service. After you've read this pamphlet, you may want to learn more about specific ethics rules. Agency ethics officials and committee management officials are there to answer any of your questions or to point you in the right direction. They will help you even after your committee has finished its work and your Government service is done.

Whether your time on a committee is short or long, understanding these basic ethics rules will make your Government service more rewarding for you and for your fellow committee members.

Government Employee Status

I will be serving on a committee only for a few days a year. Am I a Government employee just because I am a member of an advisory committee?

Not necessarily. However, if you have been given this pamphlet by the agency sponsoring your advisory committee, it's likely that you are serving as a **special Government employee (SGE)** [1] and are subject to the Government's ethics rules. An agency official should determine your employment status and then inform you whether you are serving on an advisory committee in an employee status.

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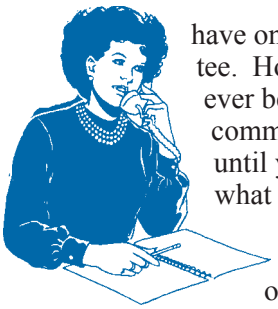
[1] *An SGE is defined as an "officer or employee . . . who is retained, designated, appointed, or employed" by the Government to perform temporary duties, with or without compensation, for not more than 130 days during any period of 365 consecutive days. See Title 18, United States Code, Section 202(a).*

In general, your status will depend upon what role you will be expected to have on the committee. It is very important for you and every member of your committee to understand your role on the committee before you even start your committee work. If you have not been told, you should ask a committee official or ethics official to explain your status so you will know whether you are subject to any of the Government's ethics rules.

If you are serving in an SGE status, you are considered a Government employee. Your role as an employee will be to provide your best judgment in committee matters that will be presented to you for discussion. As someone serving on a committee in an SGE status, you will be subject to most of the Government's ethics rules. Many of these rules will be discussed in this pamphlet.

Keep in mind that some committee members may be regular Government employees. Other members may not be serving as employees at all. These non-employee members may be serving as representatives of outside organizations. Representative members are not subject to the Government's ethics rules because they are only on a committee to provide the views of outside interest groups or stakeholders.

If you are ever unsure about your role or status on an advisory committee, talk to a committee or ethics official. In some cases, your committee appointment papers will say what your status is and/or the role you will



have on the committee. However, don't ever begin your committee work until you know what your status is going to be while serving on a committee.

Screening for Conflicts of Interest

Is there anything that I should be doing to comply with the Government ethics rules before I begin my committee service?

Yes. You'll need to get an "ethics checkup" before you begin your committee's work. We've all read press stories about athletes having to pass a physical examination before they can start playing for a sports team. One reason that teams require athletes to pass such exams is to make sure they are able to perform to the very best of their ability. In much the same way, the Government wants to ensure that you will be able to perform to the best of your ability when you begin working on one of its advisory committee teams.

Your best service is possible only when you are not affected by conflicts of interests or appearances of conflicts of interest. Conflicts of interest can arise if you have extensive outside

activities and financial holdings or other interests that relate to the subject matter of your committee service. An "ethics checkup" or a conflict of interest screening helps the Government ensure that your committee work is done in a manner that will uphold the Government's high ethical standards.

Financial Disclosure Reports

What does an "ethics checkup" involve? Is this exam a one-time event? How will I know if I have passed this ethics checkup?

As with any physical exam, there is always a little bit of paperwork to fill out. In general, one of the first forms you have to complete prior to beginning your committee work is a financial disclosure report. This report collects information about you, your spouse, and dependent children. You will have to fill this report out before you give any advice to the agency and in no event later than your first committee meeting. You will have to complete this report annually if you are reappointed.

As you know, no exam is ever complete without some amount of probing by the doctor. In much the same way, ethics officials will probe and look closely at your report to see if any of your financial interests or affiliations may raise any ethical flags. In some cases, they may have to ask you additional questions about your finances. Keep in mind that this checkup will ultimately benefit both you and your committee's work. An ethics checkup will protect you from unintentionally violating ethics laws and rules. The ethics laws can sometimes carry very serious penalties and fines if you violate them by allowing your conflicts to go untreated. This exam will help the Government ensure that your advice is free from any actual or perceived conflicts of interest.

Your agency ethics official can tell you more about the financial disclosure report, including the type of report you will be required to fill out. Even after you have filed your report, you may want to sit down and talk to your ethics official about your report if you believe your committee is going to work on a matter that may affect one or more of your financial holdings. In some cases, a matter that would raise

concerns may not have been apparent during your initial "ethics checkup." You should immediately consult with an agency official about this matter. Remember, an ethics checkup is only as good as the information you provide to your agency.

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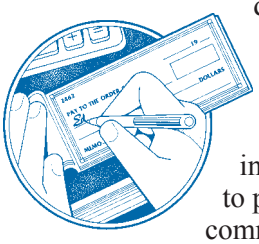
Financial Conflicts of Interest

I work for a pharmaceutical company, and over the years have received a fair amount of stock in the company. What should I do if the work of my advisory committee will affect my employer?

Generally, you may not work on a committee matter that will affect your own, or your employer's, financial interest. For example, let's say you were serving on an advisory committee that is advising an agency on whether it should continue a health program that provides nutrition information and free vitamins to children. The Government purchases some of the vitamins it distributes from your company. It would be a conflict of interest for you to participate in committee matters relating to the distribution of the vitamins, because you both own stock in, and are employed by, a company that has a financial interest in the issue.



Whether you can be involved in committee matters that relate generally to the agency's nutrition program depends on how the program will affect your company. The agency's ethics official or committee management official will advise you on how to proceed.

Financial Conflicts of Interest—Imputed Interests

Would I still have a conflict of interest if I didn't work for the pharmaceutical company or own any stock, but my spouse owned stock in the company that she bought through her broker?

Yes. The ethics laws treat the financial interests of the following as if they were your own financial interests:

- ❒ Your spouse;
- ❒ Your minor child;
- ❒ Your employer;
- ❒ Your general partner;
- ❒ An organization in which you serve as officer, director, trustee, or general partner; or
- ❒ A person with whom you are negotiating or have an arrangement for prospective employment.

So, if your spouse owned stock in the pharmaceutical company described above, you would still have the same conflict of interest concern described in the previous question.

Conflicts of interest concerns that are not addressed can penalize you and your committee's work. Ethics officials or committee officials will work with you to make sure that you can continue to do your committee work ethically and honorably.

Resolving Financial Conflicts of Interests

What steps should I take to avoid violating the Government's ethics rules if I have a conflict of interest?

There are several ways to avoid a conflict of interest while working on a committee matter. The most common way is simply not to work on a particular committee matter if it raises a conflict of interest for you. For example, in the situations discussed above, to avoid what otherwise would be a conflict of interest because of your financial interest in the pharmaceutical company, you could simply not participate in those committee matters that would affect the financial interests of the company. We call this remedy a recusal.

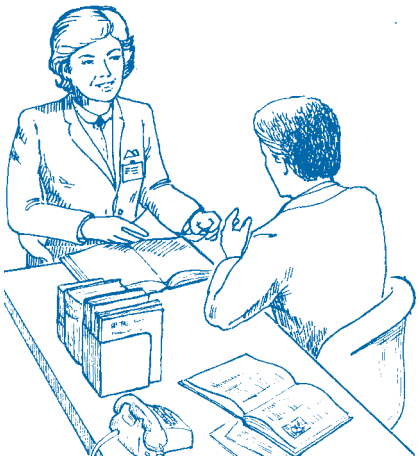
If you have a conflict of interest, you should consult an ethics official because ethics regulations may resolve some of your conflicts of interests. For example, there are some exceptions that apply if the value of your stock is below a certain amount. Another exception may permit you to participate in matters affecting your non-Federal employer in certain cases.

Considering Appearance Issues

Am I required to do anything if I have an outside business relationship that is not a financial conflict of interest, but just looks bad for my committee?

Because you serve the Government, you should always conduct yourself in a manner that is above ethical reproach. So, even if there is no financial conflict of interest, your outside relationships may at times raise questions in the public's mind about how fair you can be while working on a particular committee matter. For example, "appearance" concerns may arise when you are asked to work on a committee matter that you know may affect a member of your household or your former employer or client. In general, you should be alert for situations where—

- ❒ a former employer,
- ❒ a client of yours or your spouse,
- ❒ a person or organization with which you have some kind of business or contract relationship, or
- ❒ your spouse's employer



will be specifically affected by your committee's activities. In some cases, it may be appropriate for you not to work on a certain committee matter because of appearance concerns.

Because you are part of the Government's team, you are never alone in dealing with these kinds of appearance concerns. If you are not sure whether a potential situation could raise an appearance problem, you should stop your work on that committee matter and contact your agency's ethics official or committee official to discuss your concerns. These officials can help you address possible appearance problems.

Outside Consulting Work

I have an outside consulting business that requires me to represent clients before the Government. Is this O.K.?

In general, you may not represent another person, whether or not you are compensated for the representation, before a Federal agency or court in connection with a matter that you have worked on as an SGE. The types of representational services covered include written and oral communications, as well as making physical appearances on behalf of someone else with the intent to influence or persuade the Government.

Once you have served more than 60 days as an SGE within the previous 365 days, you may not represent anyone on any matter pending in the agency where you serve. Remember, you should always talk to an agency official if you are thinking about representing a client before the Government on a matter that involves the subject matter of your committee's work or the overall programs of the agency that is sponsoring your committee.

Standards of Ethical Conduct Rules

Are the conflict of interest laws the only ethics rules that I must know before I start my work as a committee member?

There are a number of other important ethics rules that will guide your conduct while you are serving as an SGE. Most of these rules are part of "The Standards of Ethical Conduct for Employees of the Executive Branch (Standards of Conduct)." As a committee member, you are expected to be aware of and follow these basic ethics rules while in Government service. Some of the rules you should know include:

- ***Don't accept improper gifts.***

  Don't ask for or accept gifts that are given because of your committee position or that come from certain "prohibited sources." For example, a company that does business with, or is regulated by, the agency that sponsors your committee is a prohibited source.

There are many exceptions to this general rule. Find out more about these gift exceptions by talking to a committee or ethics official.

❒ ***Don't use public office for private gain.***

For example, you may not use your committee position, title or any authority associated with your advisory committee to coerce or induce a benefit for yourself or others.

❒ ***Don't misuse Government information.***

If you get information that has not been made available to the general public, don't use (or allow the improper use of) that nonpublic information to further any private interest, either your own or another's. Contact a committee official or agency ethics official if you have any questions about whether you may release certain types of information.

❒ ***Use Government property and time properly.***

Always use Government property only for authorized purposes. Government property includes office supplies, telephones, computers, copiers and any other thing purchased with Government funds. Also, be sure to use your official time to carry out committee work.

❒ ***Don't accept compensation for teaching, speaking, and writing related to your Government duties.***

This restriction applies in narrow circumstances to SGEs. It does not apply at all if the compensation is for teaching university courses. And it applies in very limited cases if you are an SGE who is expected to serve less than 60 days. If you intend to receive

compensation for teaching, speaking, and writing that is related to the subject of your committee's work, talk to an ethics official first so that you are sure the compensation is acceptable.

❒ ***Abide by expert witness rules.***

In general, you cannot be an expert witness in a judicial or administrative proceeding if you participated as a Government employee in the matter that is the subject of the proceeding. Moreover, if you are appointed by the President, serve on a commission established by statute, or have served or are expected to serve more than 60 days in a

period of 365 days, this bar applies to any proceeding in which your employing agency is a party or has a direct and substantial interest.

The rules that govern service as an expert witness can be very complex, so you should always get advice from an agency ethics official before you agree to serve as an expert.

Other Ethics Rules

Are there any ethics rules that may limit my political activities during my service on a committee?

Yes, a law known as the Hatch Act limits certain political activities of Government employees, including SGEs when they are engaged in committee work. The law has been substantially amended to allow most Government employees to engage in many types of political activities. However, you should check with your agency ethics official to ensure your activities comply with these laws. You may also want to check the U.S. Office of Special Counsel's website (the agency responsible for enforcing this law) for more information and guidance at www.osc.gov.

Post-Employment Laws

Do any ethics rules apply to me after my service on an advisory committee has ended?

Yes. Post-employment laws may limit the types of communications you may make back to the Government on behalf of another person.

For example, you may be permanently barred by a criminal law from representing anyone else before a Federal agency or court on certain matters (such as a contract, grant or even an investigation) that you worked on while serving on an advisory committee.

There are some other restrictions that could apply to your post-Government activities, depending on your agency and the function you served in on a committee. Your agency's ethics official can help you to understand these and other post-employment rules, either before or after your committee service ends.

Some Final Thoughts

The Government is very grateful for your dedicated service. Your commitment in upholding the integrity of Government service before and even after your committee

service ends is important and will help maintain public confidence in the Government's decision making and in the quality of your committee's work.

We hope this summary helps you to understand how some of the Federal ethics rules may apply to you as a Federal advisory committee member serving as an SGE. It is now up to you to ensure that you **serve with honor** by following this game plan for successful participation on the Government's advisory team.

In you need more information, please talk to a committee management official or your agency ethics official. Like a good coach, these individuals are there to help guide you into becoming the best committee member you can be — one that acts ethically and responsibly before and after his or her service ends. In this way, you can be proud of your service to the Government and to your advisory committee team.

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SGE Game Plan for Peak Ethical Performance

1. Don't ever begin your committee work until you know what your role or status is on a committee.

2. Always get an "ethics checkup" before you begin your committee work.

3. Don't work on a committee matter that will affect your financial interests, unless some exception allows you to do so.

4. Always check with an ethics official if you have any concerns about an appearance of a conflict of interest.

5. Improve "your game" by becoming more familiar with Government ethics rules, especially those that are found in the Standards of Conduct and in the Conflict of Interest laws.

6. Talk to your agency ethics official if you anticipate doing some teaching, speaking, or writing as an outside activity for compensation or engaging in representational activity before the Government.

7. Understand the post-employment rules either before or after your advisory committee service ends.

8. Remember that learning more about the Government's ethics rules will help ensure that you serve your committee honorably.

REFERENCES

1. *NIH Guide for Grants and Contracts*. (http://grants.nih.gov/grants/guide/index.html)

2. HHS *Grants Administration Manual*. (HHS, regular issuances.)

3. NIH *Policy Manual Chapters* (http://www1.od.nih.gov/oma/manualchapters/)

4. NIH *Grants Policy Statement* (http://grants.nih.gov/grants/policy/nihgps_2003)

5. NIH Almanac, 2008.

6. *NCI 2008 Fact Book*, NCI.

7. *Orientation for the National Cancer Advisory Board*, NCI, 2009.

8. *Everything You Wanted To Know About the NCI Grants Process But Were Afraid To Ask*. NIH Publication No. 05-1222, September 2005.

9. *NIH Committee Management Handbook*. November 3, 2000.

10. *Overview of the Ethics Rules for Special Government Employees Serving on Advisory Committees*, Ethics Division, Office of the General Counsel, HHS.

RECOMMENDED WEB SITES

The following Web sites have valuable information regarding the grants process and other useful information:

Grant Writing Tips:
http://grants.nih.gov/grants/grant_tips.htm

Center for Scientific Review:
http://cms.csr.nih.gov

Submission and Assignment Process:
http://csr.nih.gov/EVENTS/AssignmentProcess.htm

Grants Process Overview:
http://grants.nih.gov/grants/grants_process.htm

Electronic Submission:
http://era.nih.gov/ElectronicReceipt/

National Cancer Institute:
http://www.cancer.gov

Extramural Funding Opportunities:
http://deainfo.nci.nih.gov/funding.htm

NCI Research and Funding: FAQs & As:
http://deainfo.nci.nih.gov/extra/extdocs/ResearchFundingQnA.htm

Grant Mechanisms and Descriptions:
http://deainfo.nci.nih.gov/flash/awards.htm

OTHER USEFUL WEB SITES

Grants.gov:
http://www.grants.gov

NCI Funding Policy:
http://deainfo.nci.nih.gov/funding.htm

Grants Guidance and Policy:
http://grants.nih.gov/grants/policy/policy.htm

NIH Guide for Grants and Contracts:
http://grants.nih.gov/grants/guide/index.html

NIH Research Portfolio Online Reporting Tool (RePORT):
http://report.nih.gov/

Extramural Training Mechanisms:
http://grants.nih.gov/training/extramural.htm

NCI Funded Research Portfolio:
http://fundedresearch.cancer.gov/

NCI Glossary of Terms:
http://deainfo.nci.nih.gov/faqs-glossary.htm

APPENDIX A

NCI SCIENTIFIC PROGRAM LEADERSHIP COMMITTEE

Dr. Harold E. Varmus
Director
National Cancer Institute

Dr. Jeffrey Abrams
Director for Clinical Research
Division of Cancer Treatment and Diagnosis

Dr. Kenneth Buetow
Director
Center for Biomedical Informatics and Information Technology

Dr. Robert Croyle
Director
Division of Cancer Control and Population Sciences

Mr. John Czajkowski
Deputy Director for Management

Dr. James Doroshow
Deputy Director for Clinical and Translational Research
Office of the Director

Dr. Joseph Fraumeni
Director
Division of Cancer Epidemiology and Genetics

Dr. Paulette Gray
Director
Division of Extramural Activities

Dr. Peter Greenwald
Associate Director for Prevention
Office of the Director

Dr. Edward Harlow
Special Advisor to the Director
Office of the Director

Dr. Lee Helman
Scientific Director for Clinical Research, CCR

Dr. Barnett Kramer
Director
Division of Cancer Prevention

Dr. Douglas Lowy
Deputy Director
Office of the Director

Dr. Alan Rabson
Deputy Director
Office of the Director

Dr. Dinah Singer
Director
Division of Cancer Biology

Dr. Sanya Springfield
Director
Center to Reduce Cancer Health Disparities

Dr. Joseph Tomaszewski
Director for Preclinical Research
Division of Cancer Treatment and Diagnosis

Dr. Edward Trimble
Director
Center for Global Health

Mr. Michael Weingarten
Director
SBIR Development Center

Dr. Linda Weiss
Director
Office of Cancer Centers

Dr. Jonathan Wiest
Director
Center for Cancer Training

Dr. Robert Wiltrout
Director
Center for Cancer Research

Dr. Barbara Wold
Director
Center for Cancer Genomics

Dr. Robert Yarchoan
Director
Office of HIV and AIDS Malignancy

Ms. Joy Wiszneauckas
Executive Secretary

APPENDIX B

OVERVIEW OF THE TYPES OF NIH FEDERAL ADVISORY COMMITTEES

• National Advisory Councils and Boards
Perform the second level peer review of research grant and cooperative agreement applications and offer advice on policy and program development.

• Program Advisory Committee
Advise on specific research programs, and future research needs and opportunities, and identify and evaluate extramural initiatives.

• Boards of Scientific Counselors
Review and evaluate the research programs and investigators of the intramural laboratories.

• Initial Review Groups (IRGs)
Provide scientific and technical merit review. This is the first level of peer review of research grant applications and contract proposals.

• Special Emphasis Panels (SEPs)
Provide scientific review of extramural applications, proposals, and concept reviews that have previously been performed through *ad hoc* groups. Provide scientific and technical merit review, which is the first level of peer review of research grant applications and contract proposals.

In addition to NCI's mandatory advisory committees, the NCI also uses: Review Groups, Working Groups, Progress Review Groups, etc.

• Review Groups
Review Groups are programmatically oriented with a clear line of reporting accountability to the National Cancer Advisory Board (NCAB) and Board of Scientific Advisors (BSA). Review Groups are charged to examine the NCI programs and infrastructures to evaluate whether changes are necessary for the Institute to be in a position to effectively guide and administer the needs of the science in the foreseeable future. That is, in reviewing and evaluating the current state of the science against what it is likely to be in the future, the groups would look at the structures the NCI has and determine whether those structures are appropriate for the future and not an impediment to the furtherance of the science. The issuance of a written report is critical to gain a consensus that the altering of a structure either is or is not necessary. The reports from the Review Groups will be presented to the NCAB and BSA for discussion and comment, and referred to the Scientific Program Leadership (SPL) Committee for follow-up and implementation.

• Working Groups
Working Groups are more fluid, responding to trans-divisional planning processes as reflected by the Bypass Budget. In the Working Group concept, staff and the extramural community engage in a free flowing forum type of discussion to identify high priority and promising scientific opportunities on the immediate horizon. No written report is envisioned. It is generally felt that the Working Groups should have a limited life span (normally 1 year unless circumstances dictate otherwise). The Working Groups, unlike the Review Groups, will not get involved in the program structure of the Institute but rather are, in essence, "think tanks," with their memberships changing over time with their major emphasis on the current state of the art of the science and identifying resources needed for optimal coordination and future progress. The Clinical Trials Working Group (http://restructuringtrials.cancer.gov/ and http://restructuringtrials.cancer.gov/files/ctwg-report.pdf) and the Translational Research Working Group (http://www.cancer.gov/researchandfunding/trwg and www.cancer.gov/aboutnci/trwg/finalreport.pdf) are examples of recent Working Groups, and reports.

APPENDIX C

PRESIDENT'S CANCER PANEL

Chair

LaSalle D. Leffall Jr., M.D. **2011**
Charles R. Drew Professor of Surgery
Department of Surgery
Howard University College of Medicine
Howard University Hospital
Washington, DC

Member

Margaret Kripke, Ph.D. **2011**
Vivian L. Smith Chair and Professor Emerita
The University of Texas
M.D. Anderson Cancer Center
Houston, TX

Executive Secretary

Abby Sandler, Ph.D.
Chief
Institute Review Office
National Cancer Institute, NIH
Bethesda, MD

APPENDIX D

NATIONAL CANCER ADVISORY BOARD

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Director of Clinical Research
Massachusetts General Hospital Cancer Center
Massachusetts General Hospital
Boston, MA

Members

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Director
Wake Forest Institute for Regenerative Medicine
Professor and Chairman
Department of Urology
Wake Forest University School of Medicine
Winston-Salem, NC

Victoria L. Champion, D.N.S. **2014**
Associate Dean for Research
Mary Margaret Walther Distinguished Professor of Nursing
Center for Research & Scholarship
Indiana University School of Nursing
Indianapolis, IN

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The Catherine Iola and J. Smith Michael Distinguished Professor of Urology
Professor of Urology/Oncology/Pathology/Pharmacology and Molecular Science
The Johns Hopkins University School of Medicine
Baltimore, MD

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University of Puerto Rico
Basic and Translational Science Director
University of Puerto Rico Comprehensive Cancer Center
San Juan, PR

Kevin J. Cullen, M.D. **2016**
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Marlene and Stewart Greenebaum Cancer Center
Professor of Medicine
University of Maryland
Baltimore, MD

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Richmond, VA

Waun Ki Hong, M.D. **2014**
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Head, Division of Cancer Medicine
Department of Thoracic/Head & Neck Medical Oncology
The University of Texas M.D. Anderson Cancer Center
Houston, TX

Mr. Robert A. Ingram **2012**
General Partner
Hatteras Venture Partners
Durham, NC

Tyler E. Jacks, Ph.D.* **2016**
Director
Koch Institute for Integrative Cancer Research
David H. Koch Professor of Biology
Massachusetts Institute of Technology
Cambridge, MA

Judith S. Kaur, M.D. **2012**
Medical Director
Native American Programs
Mayo Comprehensive Cancer Center
Professor of Oncology
Mayo Clinic
Rochester, MN

* Newly appointed member pending personnel paperwork.

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Board of Directors
University of California,
San Francisco Foundation
Los Angeles, CA

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Vice President/Global Head of Oncology
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Cancer Research
Professor of Surgery
Duke University School of Medicine
Durham, NC

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School of Nursing
Birmingham, AL

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Associate Dean for Global Health
Director, Center for Clinical Cancer Genetics
University of Chicago
Pritzker School of Medicine
Chicago, IL

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Vanderbilt-Ingram Cancer Center
B.F. Byrd, Jr. Professor of Oncology
Vanderbilt University Medical Center
Nashville, TN

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Professor and Flora L. Thornton Chair
Department of Preventive Medicine
Keck School of Medicine
Director, Institute for Global Health
University of Southern California
Los Angeles, CA

William R. Sellers, M.D. **2016**
Vice President/Global Head of Oncology
Novartis Institutes for BioMedical Research, Inc.
Cambridge, MA

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Sciences, The National Technology Program
Research Triangle Park, NC

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National Institutes of Health
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Commissioner
U.S. Food and Drug Administration
Silver Spring, MD

John P. Holdren, Ph.D.
Science Advisor to the President
Director
Office of Science and Technology Policy
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National Institute for Occupational Safety and
Health (NIOSH)
Washington, DC

Lisa Jackson, M.S.
Administrator
U.S. Environmental Protection Agency
Washington, DC

The Honorable Dr. Michael J. Kussman
Under Secretary for Health
Veterans Health Administration
U.S. Department of Veterans Affairs
Washington, DC

Anna Palmisano, Ph.D.
Associate Director, Office of Biological and
Environmental Research
U.S. Department of Energy
Washington, DC

The Honorable Kathleen Sebelius, M.P.A.
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Washington, DC

The Honorable Hilda L. Solis
Secretary
U.S. Department of Labor
Washington, DC

Inez Tenenbaum, M.Ed.
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Bethesda, MD

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Assistant Secretary of Defense for Health Affairs
The Pentagon
Washington, DC

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Medical Officer, Office of Occupational Medicine
OSHA/U.S. Department of Labor
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(The Honorable Hilda L. Solis - DOL)

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Veterans Health Administration
U.S. Department of Veterans Affairs
Washington, DC
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National Institute of Environmental Health Sciences
National Institutes of Health
Bethesda, MD
(Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S.- NIEHS)

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Division of Oncology Drugs
U.S. Food and Drug Administration
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(Margaret A. Hamburg, M.D. - FDA)

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United States Military Cancer Institute
Walter Reed Army Medical Center
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Surveillance Branch
Division of Surveillance
Hazard Evaluations & Field Studies
National Institute for Occupational Safety and Health
Cincinnati, OH
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Biological Systems Sciences Division
Office of Biological and Environmental Research
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Division of Extramural Activities
National Cancer Institute, NIH
Bethesda, MD

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Ms. Claire L. Harris
Division of Extramural Activities
National Cancer Institute, NIH
Bethesda, MD

APPENDIX E

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Institute of Technology and Harvard University
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Professor of Surgery
Department of Surgery and Pathology
Director, Experimental Therapeutics
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Duke University Medical Center
Durham, NC

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Professor of Oncology
Chair, Department Cancer Prevention and Control
Roswell Park Cancer Institute
Buffalo, NY

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Division of Health Sciences and Technology and Electrical Engineering and Computer Science
Massachusetts Institute of Technology
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Andrea Califano, Ph.D. **2013**
Director, Columbia Initiative in Systems Biology
Director, Sulzberger Columbia Genome Center
Associate Director, Herbert Irving Comprehensive Cancer Research Center
Professor of Systems Biology
Department of Biochemistry and Molecular Biophysics, Biomedical Informatics, and Institute of Cancer Genetics
Columbia University Medical Center
New York, NY

Michael A. Caligiuri, M.D. **2012**
CEO and Director
The Comprehensive Cancer Center
Ohio State University (OSUCCC)
Columbus, OH

Arul M. Chinnaiyan, M.D., Ph.D. **2015**
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Director, Pathology Research Informatics
Director, Cancer Bioinformatics
Director, Michigan Center for Translational Pathology
University of Michigan
Ann Arbor, MI

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Center for Stem Cell Biology & Regenerative Medicine
Professor of Pediatrics & Physiology
Associate Dean for Research,
University of Maryland School of Medicine
Baltimore, MD

Chi V. Dang, M.D., Ph.D. **2014**
Professor of Medicine
Division of Hematology-Oncology
Department of Medicine
Director, Abramson Cancer Center
Director, Abramson Family Cancer Research Institute
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA

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President
The University of Texas M. D. Anderson Cancer Center
Houston, TX

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Director
Mayo Clinic Cancer Center
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Professor of Pharmacology
Department of Molecular Pharmacology and Experimental Therapeutics
Mayo Clinic
Rochester, MN

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University of Pennsylvania School of Medicine
Chairman
Department of Surgery
Hospital of the University of Pennsylvania
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Associate Dean for Oncology
OHSU School of Medicine
Oregon Health and Science University
Portland, OR

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Center for Community Based Research
Dana-Farber Cancer Institute
Professor, Department of Society, Human Development and Health
Harvard School of Public Health
Boston, MA

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Professor, Nursing Research and Education
Full Member, Cancer Control and Population Sciences Program
Comprehensive Cancer Center
City of Hope National Medical Center
Duarte, CA

Kathleen M. Foley, M.D. **2013**
Attending Neurologist
Pain and Palliative Care Service
Department of Neurology
Memorial Sloan-Kettering Cancer Center
New York, NY

Sanjiv S. Gambhir, M.D., Ph.D. **2012**
Professor
Department of Radiology and Bio-X Program
Director, Molecular Imaging Program
Stanford University
Stanford, CA

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Asa & Patricia Shiverick and Jane Shiverick (Tripp) Professor of Hematological Oncology
Director
Comprehensive Cancer Center and Ireland Cancer Center
University Hospitals of Cleveland
Case Western Reserve University
Cleveland, OH

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Gordon Moore Endowed Chair
Chair, Department of Biomedical Engineering
Director, OHSU Center for Spatial Systems Biomedicine
Oregon Health and Science University
Portland, OR

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President and Scientific Director
Children's Memorial Research Center
Medical Research Institute Council Professor
Lurie Comprehensive Cancer Center
Feinberg School of Medicine
Northwestern University
Chicago, IL

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Warren Alpert Medical School of Brown University
Department of Radiation Oncology
Rhode Island Hospital
Providence, RI

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Director
Virginia G. Piper Center for Personalized Diagnostics
The Biodesign Institute
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Co-Director, Cancer Prevention and Control
Arizona Cancer Center
Professor of Epidemiology
Mel and Enid Zuckerman Arizona College of Public Health
The University of Arizona
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James L. Omel, M.D. **2012**
Education and Advocacy
Volunteer, International Myeloma Foundation
Volunteer, Multiple Myeloma Research
Volunteer, Leukemia, Lymphoma, Myeloma Society
Grand Island, NE

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Southwestern Ball Distinguished Chair in Neuroscience Research
Director, Kent Waldrep Center for Basic Research on Nerve Growth and Regeneration
Diana & Richard C. Strauss Distinguished Chair in Developmental Biology
University of Texas Southwestern Medical Center
Dallas, TX

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Morris Loeb Professor
Director, Chemical Biology
The Broad Institute of Massachusetts Institute of Technology and Harvard University
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Informatics and BioComputing Platform
Ontario Institute for Cancer Research
Toronto, Ontario, Canada

Bruce W. Stillman, Ph.D. **2012**
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Cold Spring Harbor Laboratory
Cold Spring Harbor, NY

Victor J. Strecher, Ph.D., MPH **2012**
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Department of Health Behavior and Health Education
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Professor of Genetics
Department of Genetics
The University of Texas M.D. Anderson Cancer Center
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Department of Cancer Biology
Wake Forest University School of Medicine
Winston-Salem, NC

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Erving Professor Chemistry
Department of Stem Cell and Regenerative Biology
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National Institutes of Health
Bethesda, MD

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Department of Radiation Oncology
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Ann Arbor, MI

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Wake Forest University School of Medicine
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Department of Social and Preventive
Medicine
University of Buffalo
State University of New York
Buffalo, NY

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Department of Adult Oncology
Dana-Farber Cancer Institute
Boston, MA

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Cancer Research Center of Hawaii
University of Hawaii
Honolulu, HI

Bernard Harlow Ph.D. **2014**
Mayo Professor and Division Head
Division of Epidemiology and
Community Health
University of Minnesota
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Professor of Pathology and
Laboratory Medicine
Department of Pathology
University of Pennsylvania School
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Professor and Phase 1 Clinical Director
UC Davis Medical Center
Internal Medicine/Hematology Oncology Cancer Center
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Hongzhe Lee, Ph.D.* **2016**
Professor of Biostatistics
Department Of Biostatistics and Epidemiology
University of Pennsylvania School of Medicine
Philadelphia, PA

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Chief Medical Officer and Professor
Hematology/Hematopoietic Cell Transplantation
City of Hope National Medical Center
Duarte, CA

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Professor of Cancer Genetics
Department of Medicine
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Markowitz Laboratory Case Cancer Center
Cleveland, OH

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Director
Stanley S. Scott Cancer Center
Louisiana State University Health Science Center
New Orleans, LA

Kenneth Offit, M.D., M.P.H.* **2016**
Chief
Clinical Genetics Service
Memorial Sloan-Kettering Cancer Center
Professor of Medicine and Public Health
Weill College of Medicine
Cornell University
New York, NY

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Division of Surgery
Professor, Department of Surgical Oncology
University of Texas M.D. Anderson Cancer Center
Houston, TX

David Poplack, M.D. **2014**
Director, Texas Children's Cancer Center
Elise C. Young Professor of Pediatric Oncology
Department of Pediatrics
Baylor College of Medicine
Houston, TX

Ms. Nancy Roach **2013**
Consumer Advocate
C3: Colorectal Cancer Coalition
Hood River, OR

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Albert Einstein College of Medicine
Bronx, NY

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H. Lee Moffitt Cancer Center & Research Institute
University of South Florida
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Department of Pathology
University of Southern California
Los Angeles, CA

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Professor of Dermatology and Immunobiology
Department of Dermatology
Yale University School of Medicine
New Haven, CT

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Director, Cancer Research
Robert W. Franz Cancer Research Center
Earle A. Chiles Research Institute
Providence Portland Medical Center
Portland, OR

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Surveillance and Health Policy Research
American Cancer Society
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University of Wisconsin Carbone Cancer Center
University of Wisconsin School of Medicine and Public Health
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Cancer Research and Treatment Center
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Institute Review Office
Office of the Director
National Cancer Institute
Bethesda, MD

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AARON Diamond AIDS Research Center
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University of Colorado Denver School of Medicine and National Jewish Health
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Head, Virology Division, University of Washington
Co-Director, Vaccine and Infectious Disease Institute
Fred Hutchinson Cancer Research Center
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Director, Tumor Microenvironment Program
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McArdle Laboratory for Cancer Research
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The Ohio State University College of Medicine
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Worldwide Discovery Franchise
Head for Infectious Disease
Merck Research Laboratories
Merck and Company, Inc.
West Point, PA

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Department of Pathology and Laboratory Medicine
Georgia Research Alliance Eminent Scholar
Emory Vaccine Center
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Salt Lake City, UT

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Distinguished McKnight Professor
Department of Microbiology
Center for Immunology
University of Minnesota Medical School
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Sloan-Kettering Institute
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Department of Pediatric Oncology
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Department of Microbiology
Center for Cell Signaling
University of Virginia Health Sciences Center
Charlottesville, VA

Nita Maihle, Ph.D. **2012**
Director, Program for Cancer Biology
Departments of Obstetrics/Gynecology, Pathology and Pharmacology
Yale University School of Medicine
New Haven, CT

Lynn Matrisian, Ph.D. **2012**
Professor and Chair
Department of Cancer Biology
Vanderbilt University School of Medicine
Nashville, TN

Suzanne Ostrand-Rosenberg, Ph.D. **2014**
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Baltimore, MD

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Department of Pharmacology and Cancer Biology
Duke University Medical Center
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Biochemistry
Chancellor's Professor
Department of Molecular Biology
University of California, Irvine
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Complex Carbohydrate Research Center
University of Georgia
Athens, GA

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University of Massachusetts Medical School
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Harry and Dana Hind Professor of Pharmaceutical Sciences
Departments of Pharmaceutical Chemistry and Pharmacology
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San Francisco, CA

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Howard Hughes Medical Institute
Rheumatology Division
Department of Medicine
Washington University School of Medicine
St. Louis, MO

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Harry C. Wiess Professor in the Life Sciences
Department of Molecular Biology
Princeton University
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Institute Review Office
Office of the Director
National Cancer Institute
Bethesda, MD

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APPENDIX H

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Director of Scientific and Federal Affairs
FasterCures
Washington, DC

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Cancer Advocate
Atlanta, GA

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Executive Director, Cancer Care
St. Vincent Indianapolis
Indianapolis, IN

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Advocate and Volunteer
Susan G. Komen for the Cure
Kansas City Area Affiliate
Kansas City, MO

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Co-Founder and Executive Director
Adenoid Cystic Carcinoma Research Foundation
Needham, MA

Michelle McMurry-Heath, M.D., Ph.D. **2014**
Director
Health, Biomedical Science, and Society Initiative (HBSS)
Washington, DC

Deborah Morosini. M.D. **2012**
Advocate for Lung Cancer Awareness
Oncology Pathologist
Pharmaceutical Research and Development
AstraZeneca Pharmaceuticals
Boston, MA

Phyllis Pettit Nassi, M.S.W. **2012**
Manager
Special Populations Prevention and Outreach
Huntsman Cancer Institute
University of Utah
Salt Lake City, UT

Jon G. Retzlaff, M.P.A., M.B.A. **2014**
Managing Director
Science Policy and Government Affairs
American Association for Cancer Research
Kensington, MD

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President & CEO
Melanoma Research Alliance
Washington, DC

Josh Sommer **2014**
Co-founder and Executive Director
The Chordoma Foundation
P.O. Box 4562
Greensboro, NC

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Chicago, IL

Max Wallace — **2013**
Chief Executive Officer
Accelerate Brain Cancer Cure, Inc.
Washington, DC

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Office of Advocacy Relations
National Cancer Institute, NIH
Bethesda, MD

APPENDIX I

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Department of Gastrointestinal Medical Oncology
University of Texas M.D. Anderson Cancer Center
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Pediatrics and Pharmacology
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Philadelphia, PA

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Professor of Surgery, Harvard Medical School
Brigham & Women's Hospital
Dana-Farber Cancer Institute
Boston, MA

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Associate Dean of Research
Professor of Pediatrics
Director
Center for Stem Cell Biology and Regenerative Medicine
University of Maryland School of Medicine
Baltimore, MD

Kenneth H. Cowan, M.D., Ph.D. **2012**
Director
Eppley Cancer Center
University of Nebraska Medical Center
Omaha, NE

Olivera J. Finn, Ph.D. (BSC) **2013**
Professor and Chair
University of Pittsburgh School of Medicine
Pittsburgh, PA

Scott M. Lippman, M.D. **2013**
Professor and Chair
The University of Texas M.D. Anderson Cancer Center
Houston, TX

Lisa A. Newman, M.D., M.P.H., F.A.C.S. **2014**
Professor of Surgery and Director, Breast Care Center and Multidisciplinary Breast Fellowship Program
University of Michigan Comprehensive Cancer Center
Ann Arbor, MI

David R. Parkinson, M.D.* **2011**
President and CEO
Nodality, Inc.
South San Francisco, CA

Nancy Roach (BSC) **2013**
Consumer Advocate
C3: Colorectal Cancer Coalition
Hood River, OR

Daniel J. Sargent, Ph.D.* **2011**
Director
Cancer Center Statistics
Professor
Division of Biostatistics
Mayo Clinic College of Medicine
Mayo Clinic Foundation
Rochester, MN

* Extended.

Mitchell D. Schnall, M.D., Ph.D. **2013**
Matthew J. Wilson Professor
University of Pennsylvania Medical Center
Philadelphia, PA

Peter G. Shields, M.D. **2014**
Professor of Medicine and Oncology
Deputy Director, Lombardi Comprehensive Cancer Center
Georgetown University Medical Center
Washington, DC

Joel E. Tepper, M.D. **2012**
Hector MacLean Distinguished Professor of Cancer Research
Department of Radiation Oncology
University of North Carolina
Lineberger Comprehensive Cancer Center
Chapel Hill, NC

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National Cancer Institute
National Institutes of Health
Bethesda, MD

Paulette S. Gray, Ph.D.
Director
Division of Extramural Activities
National Cancer Institute
National Institutes of Health
Bethesda, MD

Rosemarie Hakim, Ph.D., M.S.
Epidemiologist
Centers for Medicare and Medicaid Services
Baltimore, MD

Lee Helman, M.D.
Chief
Pediatric Oncology Branch
Deputy Director
Center for Cancer Research
National Cancer Institute
National Institutes of Health
Bethesda, MD

Michael J. Kelley, M.D., F.A.C.P.
National Program Director for Oncology
Veterans Health Administration
U.S. Department of Veterans Affairs
Washington, DC

Richard Pazdur, M.D., F.A.C.P.
Director
Division of Oncology Drug Products
U.S. Food and Drug Administration
Rockville, MD

Alan Rabson, M.D.
Deputy Director
National Cancer Institute
National Institutes of Health
Bethesda, MD

Executive Secretary

Sheila A. Prindiville, M.D., M.P.H.
Director
Coordinating Center for Clinical Trials
Office of the Director
National Cancer Institute
National Institutes of Health
Bethesda, MD

* Extended.

APPENDIX J

EXAMPLE OF REQUEST FOR APPLICATION (RFA) CONCEPT FORM AND JUSTIFICATION

Attachment I	**Date Prepared:__11/21/08_____**
REQUEST FOR EC/BSA CONCEPT APPROVAL **REQUESTS FOR APPLICATIONS (RFAs)/CONTRACTS (RFPs)** **Title: Cancer Intervention and Surveillance Modeling Network**	
RFA _X__ Coop. Ag. __X__ RFP____ Activity Code (e.g.R01)__U01_____ **Limited Comp. _____ New ___ Reissue _X__**	
Division/Office/Center: Cancer Control and Population Sciences **Division/Office/Center Co-sponsor(s): _____**	**Program Director: Eric J. Feuer, Ph.D.** **Division/Office/Center Director: Robert Croyle, Ph.D.**
Length of Award (Yrs.) ___5_____ **Anticipated Award Date:_09/2010____**	**Source of Funds: RPG _X__Control ___Centers____** **Other Res:_____ Construct _____ NRSA _____**
RFAs (Set Aside): **(single issuance only)** **Amount of Set Aside 01 Year:__$5.4M____**	**Est. Number of Awards :_____6_____** **Est. Cost for Total Project Period:___$29.4M_____**
Justification for Use of RFA/RFP Mechanism: **Attached: ___X_____** **Congressional Mandate:_____** **Other: _____**	**<u>New issuance</u>:** **Are evaluation criteria included? _____** **<u>Reissuance</u>:** **Is the evaluation included? __Yes_____**

revised: March 13, 2008

Justification for Reissuance
Cancer Intervention and Surveillance Modeling Network (CISNET)

I. Background

The Cancer Intervention and Surveillance Modeling Network (CISNET) is a consortium of NCI-sponsored investigators whose focus is to use modeling to improve our understanding of the impact of cancer control interventions (e.g., prevention, screening and treatment) on population trends in incidence and mortality. These models can be used to project future trends and aid in the development of optimal cancer control strategies. Currently, CISNET consists of four groups of grantees who focus on breast, prostate, colorectal, and lung cancers which utilize statistical simulation and other modeling approaches. The models incorporate data from randomized controlled trials, meta-analyses, observational studies, national surveys, and studies of practice patterns to evaluate the past and potential future impact of these interventions.

A. Continuing Scientific Need

There is a formidable and growing gap between the rapid pace of innovation in biomedicine and our ability to harness it to improve population health. While contemporary science has enabled the collection and analysis of health-related data from numerous sectors, enormous challenges remain to integrate various sources of information into optimal decision-making tools to inform public policy. Informed decisions regarding effective clinical and public health interventions for the four cancer sites in CISNET can have enormous impact because of their high incidence and mortality, and cancer control potential. Further public health challenges can be tackled by expanding work in this four cancer sites and by extending beyond these original four cancer sites.

Originally conceived as “virtual laboratories” performing in silico experiments of potential public health strategies, CISNET represents a quantum leap forward in the practice of modeling to inform clinical and policy decisions. Collaborative work on key questions promotes efficient collecting and sharing of the most important data resources, and critical evaluation of the strengths and weaknesses of each data sources. A systematic comparative modeling approach brings transparency to the modeling process. Providing results from a range of models, rather than a single estimate from one model, brings credibility to the process and reassures policy makers that the results are reproducible.

CISNET is committed to bringing the most sophisticated evidence based-planning tools to the areas of population health and public policy. CISNET models can translate evidence from randomized trials and epidemiological studies to the population setting by extrapolating evidence beyond study protocols to the general population accounting for actual usage in less controlled settings. Modeling real and hypothetical scenarios allows for the identification of key factors influencing outcomes and efficient cancer control strategies. The consortium’s work informs clinical practice and recommended guidelines by synthesizing existing, albeit often incomplete, information to model gaps in available knowledge. CISNET provides a suite of models that are able to meet the challenges of the increasing pace of scientific discovery and are poised to address emerging questions, and to determine the most efficient and cost-effective strategies for implementing technologies in the population. CISNET models can assist in determining which new technologies are the most promising when scaled up to the population level.

The research and accomplishments of CISNET to date have created a solid foundation that enables NCI and CISNET investigators and collaborating organizations to address a number of emerging cancer

control questions. However, there is an expanding scientific need for tools which assist in synthesizing emerging evidence in a timely manner due to the extraordinary pace of developments in cancer control technologies, basic science studies investigating molecular and biological determinants of cancer risk, upcoming results from clinical trials, and new health-related data. In addition, the maturation of modeling in cancer sites beyond the four covered by CISNET indicates that the time may be ripe for extensions to other cancers, e.g. cervical, esophagus, and ovarian cancer.

B. Accomplishments

i. Building Capacity and an Approach to Modeling

A major accomplishment of CISNET has been to build the capacity and an approach for comparative analysis using population-based models to answer important policy-based questions. This has included the following components:

- **Flexible broad-based disease models** CISNET models incorporate a central cancer model, which can be modified by the full range of cancer control interventions (i.e., changing risk factor profiles of the population, new screening modalities, and treatment regimens). Outputs can include the full range of the benefits and harms/costs of the interventions. Flexible models of this type can be easily adapted to incorporate new technologies as they are developed. For example, CISNET models were easily adapted to incorporate the costs, operating characteristics, and unique logistics (i.e. optical colonoscopy following a positive screen) of CTC Colonoscopy ("virtual colonoscopy").
- **Multiple birth-cohort modeling** This type of modeling captures a range of birth cohorts and changing risk factor profiles, screening behaviors, and treatments used by each cohort as it ages, allowing us to represent the impact of intervention in the actual U.S. population. There is increasing recognition that modeling a single hypothetical cohort often does not fully capture the entire impact or potential cost effectiveness of an intervention as implemented in the US population.
- **Comparative modeling** Independent modeling efforts often yield disparate results that are difficult to reconcile. A comparative modeling approach explores differences between models in a systematic way. Comparative modeling produces a range of results across models and, when consensus can be reached, greatly enhances the credibility of modeling results by highlighting their reproducibility. When results are disparate, it can help to pinpoint areas where our knowledge base is insufficient and further research is needed. CISNET has been cited by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force on Good Modeling Practices for its role establishing a forum that enables modelers to compare results and articulate reasons for discrepancies (Weinstein et al, Value Health, 2003).
- **Transparency in modeling and assumptions** CISNET has developed and implemented standardized model documentation. Model profiles (available online at http://cisnet.cancer.gov/profiles/) are standardized descriptions that facilitate the comparison of models and their results. Users can read documentation about a single model or read side-by-side descriptions that contrast how models address different components of the process. Journal articles seldom contain extensive model descriptions; links from publications to model profiles provide a more complete model description.

ii. Outreach and Collaboration

To achieve the full goals of CISNET, a core value has been to make the research and policy

communities aware of the existing modeling capacity/approach and to encourage active collaborations. CISNET initiated a series of webinars to encourage discussions with colleagues in the fields of advocacy, public policy, legislative affairs, cancer control planning, and clinical science on the potential use of CISNET's decision support tools to guide evidence-based recommendations and cancer control planning. Examples of groups which CISNET has collaborated with include the U.S. Preventive Services Task Force, the Center for Medicare and Medicaid Services, the Division of Cancer Prevention and Control of CDC, and the American College of Radiology Imaging Network.

iii. Scientific Accomplishments

CISNET investigators have contributed significantly to answering research questions related to modeling the natural history of cancer, performed analyses to synthesize results from both controlled trials and observational studies, and applied their models to answer policy-relevant questions. These research accomplishments can be seen in more than 135 papers published individually and collectively. Examples of completed/ongoing work include:

- A landmark study published in the NEJM reported that the significant reductions in breast cancer mortality from 1975-2000 could be attributed about equally to mammography and adjuvant therapy. This was a case where observational data (combined in a novel way using seven different models) helped confirm mammography benefits when controlled trials alone could not settle the debate (Berry DA et al., New Eng J Med 2005).
- Decision analyses for the US Preventive Services Task Force in breast cancer and colorectal cancer to assist recommendation revisions with respect to age to begin screening, age to end screening, intervals of screening, and the relative benefits of different modalities of colorectal cancer screening. These analyses were able to effectively supplement the standard evidence reviews commissioned by the task force (Zauber AG et al., Ann Intern Med 2008).
- A colorectal cancer mortality projections website which projects future trends and evaluates how potential increases in prevention, screening, and access to state-of-the-science treatment may affect future mortality trends (http://cisnet.cancer.gov/projections/colorectal/). It is intended for policy, legislative, and cancer control planning staff at the federal, state, and local levels, as well as advocacy and professional groups.
- Technology assessments requested by the Center for Medicare and Medicaid Services as part of National Coverage Determinations for the immunochemical fecal occult blood test, DNA stool test, and CT colonography (http://cisnet.cancer.gov/colorectal/highlights/cms_report.html).
- An analysis of the cost effectiveness of CT colonography in collaboration with the American College of Radiology Imaging Network based on the results of their National CT Colonography Trial (ACRIN 6664).
- Quantifying the potential harms and benefits of CT screening for lung cancer. This comparative simulation of the Mayo CT lung study will help to better frame the debate concerning CT screening by conceptually linking specific outcomes to underlying proposed models of the natural history of lung cancer and the operating characteristics of CT screening.
- A study quantifying the potential of screening high-risk populations for lung cancer based on their genetic susceptibility (Gorlova OY et al., Hum Hered 2003).
- Reconciling different estimates of lead time and overdiagnosis due to PSA screening. Prior estimates were highly disparate because they were developed under differing systems of practice of PSA use, different populations, as well as under different assumptions and definitions of lead time and overdiagnosis. CISNET investigators brought order to this disparate literature by developing

estimates using US practice patterns and a consistent set of definitions (Draisma G. et al., J Natl Cancer Inst, In Press).

- A study using competing models of the natural history of prostate cancer found that the models which incorporated the possibility of tumor dedifferentiation during the preclinical phase provided a better fit to data from the European Randomized Trial on Screening for Prostate Cancer (ERSPC), indicating that screening with PSA and early treatment can possibly prevent progression to poorer Gleason's score (Draisma G et al., Int J Cancer 2006).

For further information on these and other CISNET accomplishments see the recently published CISNET booklet (NIH Pub. No. 09-7354, December 2008, and http://cisnet.cancer.gov).

II. Purpose of the RFA

The purpose of the RFA is to expand and extend the work of CISNET in a systematic manner. Four commonly identified phases of the translation of medical research from initial discovery to population impact include: T1 – discovery to health application, T2 – health application to evidence-based practice guidelines, T3 – practice guidelines to health practice, and T4 – health practice to population health impact. CISNET models provide a platform for evaluating the potential downstream consequences of decisions and strategies that are made in earlier phases, and thus can be an effective tool for helping to optimize choices. Thus, the purpose of the reissuance of the CISNET RFA is to explore the following areas where modeling can assist in optimizing the flow of the translation of cancer research:

Multi-scale modeling: Bridging the gap between models developed at the molecular/cellular level and CISNET models which go from the tumor growth to the population level can help extrapolate the potential impact of basic science discoveries (e.g., mechanistic models of the action of drugs at smaller scales validated against clinical trials). Two pilot projects to integrate models developed in NCI's Integrative Cancer Biology Program (ICBP) with CISNET models are underway and a workshop is planned to bring the CISNET and ICBP communities together. Efforts of this type may help prioritize those basic science developments that show the most promise for population impact. For more information on ICBP see http://icbp.nci.nih.gov/.

Incorporating genomic and family history risk profiles: Utilizing risk profiles that are based on family history and genomic information has the promise of more effectively targeting prevention, screening, and treatment efforts. Incorporation of information on family history, genomics, and gene–environment interactions into cancer models provides a platform for fitting together the pieces of this complex puzzle as it becomes available. Because we are in a rapidly developing state of knowledge with many gaps, modeling helps make assumptions about complex phenomenon more explicit and exposes the most important "leverage points" where knowledge gaps exist. The impact of awareness and appropriate usage of genetic screening tests among both physicians and the general public can also be included in modeling efforts.

Upstream modeling: Most CISNET models start with risk factor trends, screening behavior, and diffusion of new treatment advances. Upstream modeling can add the social, political, cultural, economic, and individual determinants of risk factor changes, screening behavior, and treatment choices. These determinants put the models a step closer to the specific policies and programs that can help modify these factors in the future, and help evaluate specific programs. Upstream modeling efforts need not be developed *de novo*, and instead CISNET can integrate existing models or use outputs from other models as input into CISNET models.

Comparative Effectiveness and Downstream Modeling: In 2007 the Congressional Budget Office issued a report advocating research on the comparative effectiveness of medical treatments. Comparative effectiveness is a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. In 2005 AHRQ was authorized to conduct and support research on the outcomes, comparative clinical effectiveness, and appropriateness of health care items and services (including prescription drugs). The idea is to focus on what is known now, ensuring that individual choices and programs benefit from past investments in research and what research gaps are critical to fill. Modeling can assist in extending current evidence from intermediate to long term outcomes, and helping to balance trade-offs (e.g. in prostate cancer treatment radical prostatectomy has been shown to have a survival advantage over watchful waiting, but has tradeoffs in terms of greater urinary and sexual dysfunction). While most CISNET models include choices of first line treatment, few include anything beyond that in terms of post diagnostic sequelae. Modeling can include important issues with respect to choices and quality of care in post diagnostic surveillance, treatment choices at failure of first line therapy or recurrence, etc.

Evaluation of Diagnostics Tests: Empirical studies of the impact of diagnostic test utilization on patient outcomes are rarely done, because of both methodologic and resource considerations. CISNET methods developed in the context of screening could be adapted for use in the diagnostic context and thus provide methods for synthesizing available information from all sources in order to make credible projections about the potential impact of the use of diagnostic tests in clinical practice and to estimate their cost-benefit profile.

Optimizing Biomarker Development Strategies: Biomarker development proceeds in five phases: Phase I – discovery, Phase II – validation, Phase III – detect disease in serum from longitudinal cohorts, Phase IV – prospective screening studies on biomarker performance in large populations, and Phase V – large scale studies to evaluate the role of biomarkers for cancer detection and overall screening impact. Each phase costs significantly more than the prior phase, but yields more information about the operating characteristics and impact of the biomarker. CISNET modelers will explore how early in the development process reasonable models of the potential cost effectiveness can be developed, thus assisting in decisions of selecting the most promising biomarkers. CISNET investigators recently participated in all four cancer site working groups of the Division of Cancer Prevention's Early Detection Research Network (EDRN) at their annual meeting, and pilot projects will be initiated to explore areas of joint interest (http://edrn.nci.nih.gov/). CISNET models can provide a tool for EDRN investigators to project the likely impact of screening tests of given sensitivity on disease-specific deaths, investigate how early in the preclinical period the test needs to become sensitive in order to produce a target benefit in terms of lives saved, given specified test characteristics, project benefits and costs associated with different regimens of screening.

Suggesting optimal routes to reducing health disparities: Models can move beyond the standard racial/ethnic characterizations, and data sources can be linked to allow modeling as a function of disparities in income/education, insurance status, and geography. Disparities and their downstream consequences can be studied in terms of smoking rates, obesity, and other risk factors; screening rates; follow-up to abnormal screening; treatment; and quality of care.

Translation of trial results into clinical guidelines and public health policy: The translation of trial results into guidelines and policy recommendations can be facilitated by modeling. In the next several years this will likely increase as trial results for PSA screening and CT screening for lung cancer in the

United States and Europe become available. For both prostate and lung cancer screening, substantial overdiagnosis and mortality benefits may coexist, complicating population-level recommendations. Trials in different countries are run under different protocols, and modeling may hold the key to translating results from one trial setting to another in order to reconcile putative differences. For example, the European Randomized Study of Screening for Prostate Cancer (ERSPC) is an "efficacy" trial with an established protocol for follow-up of abnormal results while the US PLCO trial is an "effectiveness" trial, with abnormal screening results provided to patient's physicians, who determine further workup. CISNET will work to produce a more seamless link between trialists, modelers, and guideline-setting organizations.

Interactive policy-level decision-making tools: Development of interactive interfaces for models that will allow cancer control planners and policy makers to explore the impact of varying key parameters involved in their decision-making options. These tools will facilitate evidence-based decisions, while ensuring that they are understandable and relevant for the target audiences.

III. Current Portfolio Analysis

Besides CISNET there are very few grants in the NCI portfolio on population based disease modeling, and nothing else which employs the rigorous comparative modeling approach. The CISNET consortium has encouraged affiliate membership for those funded under a different mechanism, but who wish to join the collaborative activities for a particular cancer site. In addition to six grants by CISNET affiliate members, we could find only three other funded grants in population level cancer modeling (on HPV vaccination, economics of colon cancer screening, and radon policy for lung cancer control).

IV. Justification for the Use of the RFA Mechanism

The RFA mechanism will continue to greatly enhance the quality and quantity of work being conducted in this still relatively untapped but high priority area. It will provide assurance that the NCI's investment to date in building the capacity for comparative population modeling is capitalized in a timely and efficient manner. An RFA will continue to enunciate the Institute's interest in models of the population impact of cancer control interventions, by increasing the available funding specifically allocated to this area, and by assembling a special review group with appropriate specialized but multi-disciplinary expertise. The special review criteria encompassed in an RFA are necessary to ensure that grantees address the priority needs of the NCI in this area and that grantees are willing and able to collaborate with each other and with NCI staff. Other mechanisms, e.g. a Program Announcement with Review (PAR), would not allow for the level of scientific interactivity desired between the grantees and with NCI. The use of the cooperative agreement mechanism (see section V) will facilitate coordination and collaboration of this work, resulting in synergistic contributions to research progress in this area, and will produce research work that can inform national and local policy in the area of cancer control and surveillance**.**

V. Justification for the Use of the Cooperative Agreement Mechanism

CISNET will be continued to be funded through a cooperative agreement (U01) mechanism. A Cooperative Agreement Mechanism will make it possible to continue to have close collaboration between NCI staff and grantees, as well as among grantees. Collaboration will: (1) facilitate comparative analyses which improve the credibility of individual models, (2) allow modeling groups access to a broader array of data resources and multi-disciplinary expertise not readily found in any

individual research center, and (3) provide a forum for discussions of validation and other methodologic issues across the consortium. Close collaboration and coordination with NCI staff is crucial because: (1) DCCPS has a federal-level function to respond to evolving surveillance and cancer control questions of national policy relevance, and can actively engage the consortium to help respond to these issues, (2) DCCPS has unique knowledge of and can help expedite access to a wide variety of data resources, and (3) the cooperative agreement mechanism will ensure substantive NCI involvement in attaining research goals and catalyzing collaborations both between consortium members and with outside groups seeking collaborations (who often come to NCI seeking assistance).

For each cancer site, we propose linked applications (each with approximately 2-5 models included), which will facilitate several goals of this reissuance, including: (1) group proposals will incorporate plans for joint collaborative analyses, rather than having to change plans after the grants are awarded, (2) the group as a whole would try to provide complete coverage of the new areas of model development (with each group specializing in certain areas), rather than each individual PI's unrealistically trying to cover the entire range of new areas, (3) since the application process would allow PI's to decide who they want to work with, it will reward those who are most cooperative, and (4) coordination of group activities would be built into the application, rather than having it funded separately. Coordination in the application phase will yield groups which have agreed upon areas for joint comparative analyses, and complementary areas of specialization. Groups can bring in specialized modeling expertise (e.g. multi-scale modelers, upstream modelers). Linked applications will designate one PI as the coordinator.

VI. Budget

We propose funding up to 6 cancer-site specific groups of linked applications averaging $900K total cost per year. The awards could be made for up to 5 years. In addition, in years 2-5 we are requesting $600K per year for discretionary core collaborative study funds that will be used to facilitate collaborations with organizations (either governmental or non-governmental) that bring timely cancer control issues to CISNET amenable to modeling (e.g. release of the PSA screening results from PLSO, with potential partnerships with trialists and the USPSTF). Funds will be used to pay for both the time of CISNET investigators, the time of collaborators, data acquisition and preparation costs, etc. These funds will be part of the coordinating PI's budget, and will be allocated with agreement of the PI's and the CISNET program director. Thus the total funding requested is:

	FY10	FY11	FY12	FY13	FY14
Grant funds	$5.40M	$5.40M	$5.40M	$5.40M	$5.40M
Core Collaborative Study Funds	_____	$0.60 M	$0.60M	$0.60M	$0.60M
Total	$5.40M	$6.00M	$6.00M	$6.00M	$6.00M

The original CISNET RFA supported two phased in rounds of funding. In September 2000, CA-99-013 funded seven grants in breast cancer and one apiece in prostate and colorectal cancer. A second round, funded under CA-02-010 in August 2002, funded 5 grants in lung cancer as well as two additional grants for colorectal cancer and one in prostate cancer. The total amount of funding under these announcements was $13.1M. In September 2005 CA-05-018 funded 15 grants (3 prostate, 3 breast, 4 colorectal, and 5 lung), and the total amount of funding to date under this solicitation is $14.6M. While the first rounds of funding focused on model development, the second round has focused on applying the models to answer

vital questions related to emerging cancer trends, the potential impact of interventions on future trends, and the identification of optimal strategies for reducing the cancer burden.

The CISNET grants have been run efficiently with an average annual budget of $0.25M total cost per awarded grant, and an average annual cost of between $3M and $4M for the entire consortium per year. With over 135 publications, CISNET participants continue to produce an exemplary publication track despite the increased time commitment of comparative modeling as opposed to single model publications. There has been a natural transition over the funding period from more technical modeling papers to papers focusing on model applications of the public health impact of interventions. Interdisciplinary expertise has been shared across the consortium, including specialized clinical and statistical expertise. The work of the consortium in facilitating evidence-based public health guidelines (e.g. ages to start and stop screening, periodicity of screening) has the potential to save billions of dollars in terms of health care costs because of the elimination of excessive testing with marginal benefit.

VII. Evaluation

An external review committee consisting of Dr. Alice Whittemore (Stanford University), Dr. Constantine Gatsonis (Brown University) and Dr. J. Sanford Schwartz (U. of Pennsylvania) have reviewed the accomplishments of CISNET to date, and indicated that the consortium has made major progress towards it primary goals. The report endorsed the areas for future research, suggested pilot projects as a way to incrementally gain experience in these new areas, and suggested evaluation of diagnostic tests as a fruitful area for modeling (which has been added). The report is attached.

In future evaluations of CISNET, the consortium should show evidence of:

- Providing an environment that is conducive to sharing modeling issues, discussing the strengths and limitation of various data sources, and collaboration.
- Providing model transparency through standardized model documentation that can be displayed on the web, and encourages cross-model comparisons of model structure and assumptions.
- Further development and utilization of multiple cohort population models that can describe the actual US population over time.
- Engaging in collaborations with relevant trialists, researchers, and policy and guidelines setting organizations.
- Providing assistance in facilitating the translation of medical research in the T1 to T4 schema in the areas identified in the “Purpose of the RFA” section above, and in other relevant areas.
- Being responsive to emerging cancer control issues.

APPENDIX K

EXAMPLE OF RFA REISSUANCE JUSTIFICATION LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

Dear BSA members,

It is our privilege to present for re-issuance the NCI's Integrative Cancer Biology Program (ICBP) RFA. The ICBP, which is the NCI's major effort in cancer systems biology, was initially funded in 2004 and currently supports 9 centers (6 full and 3 planning centers). The interdisciplinary centers each focus on different aspects of cancer biology, but they all utilize a comprehensive or systems approach relying on mathematical modeling and computer simulation.

Along with the proposed re-issuance concept, we are including the independently commissioned evaluation report and a CD containing the latest progress reports from each of the centers describing their recent scientific progress. As you review this material, please note that three of the centers (Case, MGH, and Stanford) were funded at the reduced level of Planning Centers. For your reference, the ICBP minisymposium presented at the last BSA meeting in June can be viewed at the following URL: http://videocast.nih.gov/launch.asp?14576. (The ICBP presentation begins at 01:37:45.)

While the proposed concept is designed to build on and extend the success of the existing program, it provides for the inclusion of new approaches and expertise by calling for a full, open competition. Early in the development of this program, it was recognized that systems biology is an emerging area of cancer research that requires sustained interdisciplinary training and research in order to translate new discoveries and models in cancer. It is for this reason that the ICBP also has maintained a significant educational and outreach component in the proposed concept. Thus, the concept we are proposing maintains the same overall structure that has already proven to be successful. Each center will be built around an important cancer issue using experimental systems biology coupled with mathematical modeling and will enhance the field with appropriate educational activities. The new program will have the following features:

- Collaborative centers (Centers for Cancer Systems Biology) composed of interdisciplinary research teams
- Co-PIs representing experimental and computational/mathematical components
- Increased emphasis on predictive computational/mathematical models and their application in experimental and translational research
- Pilot projects in biology, mathematical modeling, and computer simulation
- Continued NCI involvement to ensure leveraging of institutional and NCI supported resources

This Program will ensure continued advances in cancer systems biology that will result in understanding and managing the complexities of cancer. We appreciate your efforts in reviewing this concept and look forward to answering any questions you may have.

Dan Gallahan, Ph.D.
Program Director
Deputy Director, DCB

Dinah Singer, Ph.D.
Director
Division of Cancer Biology

APPENDIX L

EXAMPLE OF REQUEST FOR PROPOSAL (RFP) CONCEPT FORM AND JUSTIFICATION

Attachment I **Date Prepared: April 28, 2009**

REQUEST FOR EC/BSA CONCEPT APPROVAL
REQUESTS FOR APPLICATIONS (RFAs)/CONTRACTS (RFPs)

Title: Developing Necessary Reagents to Enable Translation of TCGA and TARGET Discoveries

RFA ___ Coop. Ag. ____ RFP_X__ Activity Code (e.g.R01)_____

Limited Comp. _____ New _X_ Reissue _____

Division/Office/Center: __CSSI_____ **Division/Office/Center Co-sponsor(s): _____**	**Program Director 1: _____** (Signature) **Program Director 2: _____** (Signature) **Division/Office/ Center Director: _____** (Signature)
Length of Award (Yrs.) ___2_____ **Anticipated Award Date:_2010___**	**Source of Funds: RPG ___Control ___ Centers____** **Other Res:__X___ Construct _____ NRSA _____**
RFAs (Set Aside): (single issuance only) **Amount of Set Aside 01 Year: $2,500,000**	**Est. Number of Awards :____4-7_____** **Est. Cost for Total Project Period:___$5,000,000_____**
Justification for Use of RFA/RFP Mechanism: Attached: ___Yes_____ **Congressional Mandate:___No_____** **Other: _____**	**New issuance:** **Are evaluation criteria included? __Yes___** **Reissuance:** **Is the evaluation included? _____** *(Large infrastructure only)*

Overview:

The Cancer Genome Atlas (TCGA) and Therapeutically Applicable Research to Generate Effective Treatments (TARGET) projects, Center for Strategic Scientific Initiatives (CSSI), Office of Cancer Genomics (OCG) are leading extramural efforts to provide a comprehensive characterization and sequence analysis of adult and pediatric cancer genomes. The comprehensive characterization by these projects, performed by large teams of extramural investigators, includes expression profiling, identification of chromosome copy number alterations, methylation changes and target gene sequencing to identify mutations. TCGA and TARGET initiatives uniquely make emerging high quality project data freely available to the community. Both projects have recently published their first successful integrated analysis of multi-dimensional genomic data (references 1-2). These findings demonstrate that high-throughput large-scale cancer genome characterization and analyses of statistically robust numbers of tumor and normal samples can produce valuable insights into the specific genes and pathways disrupted in specific cancers. Moreover, these multi-dimensional data sets offer significant opportunity to empower individual investigators to study the relationships between these genomic changes at all levels and their impact on the biology of specific cancers. Both TCGA and TARGET portend a new generation of molecularly-based cancer interventions.

To leverage data from TCGA and TARGET requires broad engagement of the cancer research communities to conduct *the in vitro* and *in vivo* studies needed to understand the correlation with these genomic aberrations with the cancer biology. Currently, this progress is blocked by a critical lack of specialized reagents and assays to bridge genomic data and clinically relevant biomarkers. This concept from CSSI (OCG and the Clinical Proteomics Technology for Cancer - CPTC) proposes to address this barrier through the development of the tools needed (reagents, assays, etc.) and pipeline that will ultimately connect the data from these projects with cancer biology and ultimately drive biomarker discovery.

Background:

Although significant advances have been made in understanding human cancer, current diagnostic and prognostic methods rarely include molecular analyses that could augment clinical data including tissue type, stage, grade and size. The team-based analysis of statistically robust numbers of samples employed by TCGA and TARGET have demonstrated that high-throughput molecular profiling of biological samples at the genomic, transcriptomic and epigenomic levels significantly enable a more complete understanding of phenotypic variations, specific genomic aberrations, and perhaps of greatest significance, the affected pathways.

However, identifying specific genetic or epigenetic changes associated with a specific cancer or cancer subtype is only the first step in determining the biological relevance of such changes. TCGA and TARGET are systematically identifying genetic alterations (e.g. mutations and copy number variation) and genes with aberrant expression levels that

are associated with human cancers. By performing this analysis across multiple different tumor types, these projects will identify potential "molecular signatures" that distinguish tumors and subtypes. An open question is whether any of these genetic changes, alone or in combination, can potentially serve as clinically useful biomarkers.

Placing these genomic changes in the context of the biology of cancer is the critical next step beyond TCGA and TARGET; which requires studies that have the potential to directly determine the functional relevance of statistically significant genomic signatures identified in these large scale efforts. To date, no systematic studies have been reported that directly correlate these significant genomic signatures with the derivative corresponding proteins. A significant barrier in determining these corresponding proteomic signatures is the lack of appropriate resources; specifically the high quality multiplex nucleic acid assays and protein-based reagents that directly target cancer-specific alterations. This lack of specific, sensitive and multiplex assays and reagents must be addressed in a timely fashion to begin the process of building a discovery pipeline from the wealth of data being generated by projects like TCGA and TARGET. This proposal will initiate the creation of such a pipeline (Figure 1) for the generation of assays and reagents that will be critical for the eventual assessment of the valuable hypotheses generated by TCGA and TARGET genetic data.

Goal: The goal of the proposed pilot program is to translate genomic discoveries from TCGA into genomic and proteomic reagents and resources that can be utilized by the scientific community to study the biological function of these alterations in tumor pathogenesis; and in doing so provide a firm foundation for the identification and validation of useful biomarkers.

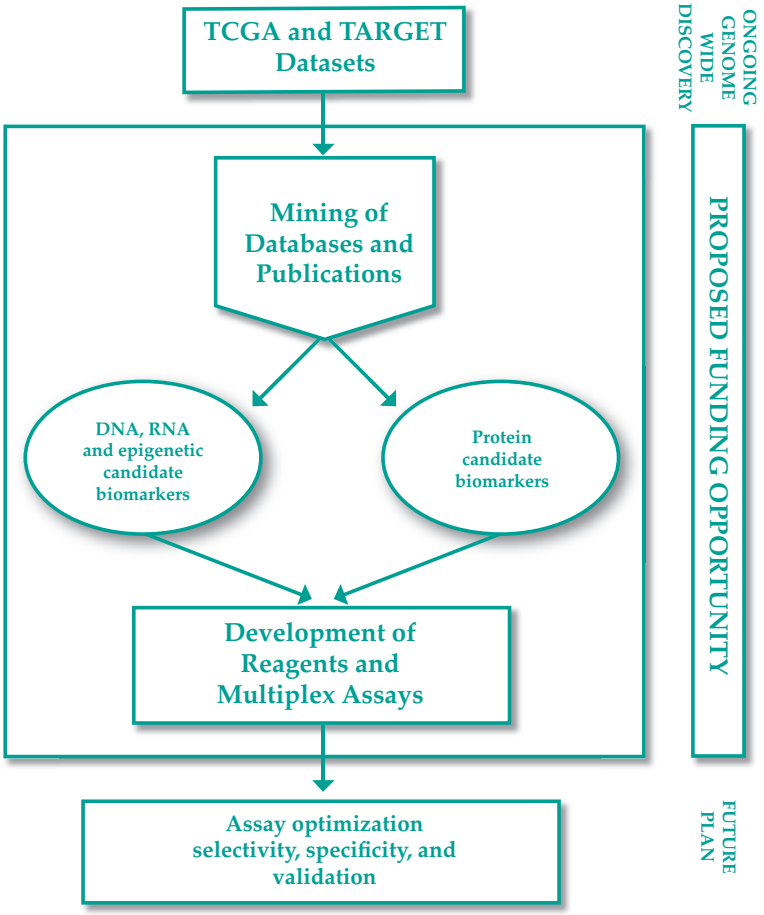

Figure 1. *Schematic of pipeline for generating biomarker reagents from cancer genomics datasets.* Scientists participating in TCGA and TARGET are depositing massive datasets to public databases on adult and pediatric tumor types. In the proposed concept, scientists will mine the genetic data for targets that may specifically serve to characterize specific tumors. These potential biomarkers might be either at the nucleic acid level or protein secreted in the bloodstream. Groups will work to identify targets, determine whether nucleic acid or protein-based tools are most appropriate, and develop reagents and assays needed to assess utility of each target as a biomarker. Reagents and information about assays developed will be available to the research community to continue to develop, improve and transfer for use in more clinically relevant applications, as appropriate.

Data from TCGA (glioblastoma multiforme and serous cystadenocarcinoma) and TARGET (acute lymphoblastic leukemia and neuroblastoma) projects are already

publicly available with data from additional samples and tumor types being added at regular intervals. The goal of this pilot project is to generate reagents and molecular-based assays that will facilitate assessment of nucleic acid and protein biomarkers based on data from both TCGA and TARGET and published data utilizing similar high quality, statistically robust data. The groups/individual investigators that are selected to generate these resources for the community will work with OCG and CPTC in CSSI during the process of target selection to ensure clear justification of the selection criteria of the specific aberrations pursued for their potential biomarker utility. Specifically, target selection will be a continuous collaborative process that leverages all valid, statistically significant data in the literature as well as data from TCGA and TARGET databases.

Purpose of Concept and Proposed Funding:

Proposed activities:

Two general classes of reagents will be generated in this project:

Nucleic Acid Reagents and Assays: Nucleic acid-based biomarkers have been identified for some cancers and have a proven track record of having significant clinical relevance. For example, breast cancer patients with HER2 amplification respond to Herceptin treatment. In glioblastoma (GBM) hypermethylation of the *MGMT* promoter has been associated with a better patient response to temozolomide treatment, the standard GBM therapy (reference 1). The comprehensive nature of TCGA and TARGET will make it possible to identify novel targets that may have potential utility as biomarkers. A few examples of potential activities that could be funded in this project include, but are not limited to:

- Development of complex genomic characterization assays for the detection of homozygous deletions and amplifications in patient samples (paraffin embedded tissue, flash frozen samples etc)
- Development of complex genomic characterization assays for quantitative real-time PCR measurement of somatic mutations, gene expression alterations or DNA methylation changes
- Development of micro-array or sequence-based methods for the simultaneous detection of many genetic alterations, gene expression variations or DNA methylation changes

Protein-Based Reagents: It is anticipated that changes at the genetic and epigenetic levels may ultimately be translated at the protein level (reference 3). The discovery that tumors can "leak" proteins and other biomolecules into the blood has led to the development of blood tests that measure the levels of these molecules in the plasma. These types of tests have sporadically served, albeit often non-specifically, as proxies for disease states in cancer patients. For example, serum CEA (carcinoembryonic antigen), is found in the serum of patients with colon, breast and lung cancers while Prostate Specific Antigen (PSA) is measured as a step in the diagnosis of prostate cancer (reviewed in reference 4). It is interesting to note that these biomarker-assay tools are all designed to wild type

versions of these proteins. Thus, generation of reagents that specifically recognize altered proteins will add to our battery of valuable reagents in the search for valid biomarkers. The current CPTC antibody characterization program develops highly characterized monoclonal antibodies to human proteins associated with cancer for the research community. All antigens and antibodies are expressed, purified, produced and characterized using standard operating procedures (SOPs) and freely accessible to the public. The pipeline developed by CPTC can therefore be leveraged for this new program that will include the development of reagents designed to specifically target mutations identified from the TCGA and TARGET datasets.

Examples of potential activities for the generation of protein focused reagents include:

- Generation of Protein Capture Reagents: Monoclonal antibodies (mAbs) directed to recognize TCGA- or TARGET-derived gene aberration targets that are specific to that mutation will be generated. Evidence for such specificity needs to be demonstrated (e.g. Western blotting, immunofluorescence analysis, immunohistochemistry, epitope mapping).
- Generation of Peptide Capture Reagents: A novel and powerful new quantitative mass spectrometry technology uses novel anti-peptide monoclonal antibodies that enable individual researchers to measure a defined set of low abundance human proteins in biological samples with sensitivity and specificity, high-throughput and cost levels that enable study of meaningfully large biological populations. This approach is also useful when the isolation of the antigen is difficult or time consuming, or when the antigen is a member of a large protein family. Therefore, to enhance application of these assay platforms, anti-peptide mAbs specific to proteotypic peptides derived from target protein and specific to the TCGA-derived gene aberration will be produced. Additional monoclonal antibody characterizations should also be demonstrated.

In summary, the deliverables of this concept include:

1. The identification of nucleic acid and protein potential biomarker targets from TCGA and TARGET data that merit further exploration
2. Generation and qualification of reagents and assays which can then be validated by the research community as potential biomarkers
3. Generation of an accessible, transparent catalogue of credentialed reagents to the research community
4. Deposition of all information developed in a publicly accessible website designated and supported by the NCI

Current Portfolio Analysis:

The National Cancer Institute (NCI) has a rich portfolio of active research in the area of cancer biology. In an attempt to identify potential areas of overlap and maximize synergy with other NCI endeavors, we performed a thorough analysis of programs within the Institute. Additionally, we investigated initiatives outside the NCI proper, including initiatives from the National Center for Research Resources and the Interagency Modeling and Analysis Group. Our portfolio analysis and review of publicly accessible information clearly indicates that this proposal will initiate a unique, systematic and focused approach to translate genomic discoveries from TCGA and TARGET into high-quality, characterized reagents that are valuable to the cancer biology community. Our analysis also indicates that there is no overlap between the proposed project and existing NCI programs (Table 1).

Table 1. *No Overlap Exists Between Proposed Program and Existing NCI Initiatives*

Program Name	Brief Description	Overlap
Innovative Molecular Analysis and Technologies Program (IMAT)	Developing creative methods and tools to understand, prevent, diagnose and treat cancer.	No
Strategic Parterning to Evaluate Cancer Signatures (SPEC)	Compile and characterize potential validity of cancer molecular signature data	No
Division of Cancer Treatment and Diagnosis (DCTD)	Identify promising areas of science and technology to improve clinical applications	No
Early Detection Research Network (EDRN)	Creation of validated biomarkers for large-scale clinical testing	No
Mutant Mouse Regional Resource Centers from the NCRR	Development of mouse models specific to certain mutations	No
In silico Research Centers (ISRCE)	Bioinformatics centers to mine data to add scientific value to datasets	No
Cancer Intervention and Surveillance Modeling Network (CisNET)	Statistical modeling to generate model that guide public health research	No
Integrative Cancer Biology Program (ICBP)	Generation of predictive computation models of cancer	No
Tumor Micro Environment Network (TMEN)	Improving our understanding of the role of tumor microenvironment in cancer initiation and progression	No
Interagency Modeling and Analysis Group (IMAG)	Development of multiscale models of the physiome in human health and disease	No
Mouse Models of Human Cancers Consortium	Development and evaluation of mouse models of human cancers	No

NCI Characterization Centers	Conducting molecular characterization of biological samples (cells and biospecimens)	No

While no ongoing programs directly coincide, we have identified examples of research that could leverage the resources generated by this proposal in their own work, thus maximizing the return on this investment. The objectives of the NCI-based programs listed above intersect with the objectives described in this proposal and would therefore directly benefit from the reagents generated by the work proposed here. These objectives and programs include:

- *Identification of Novel Cancer Biomarkers*: Two programs in the NCI portfolio that will directly benefit from the reagents generated include The Innovative Molecular Analysis Technologies (IMAT) Program and the Early Detection Research Network (EDRN). Each program could directly utilize the resources generated to expedite reaching their overarching objectives which include the identification and validation of biomarkers. Because our proposal focuses on generating reagents and assays targeting mutations or other cancer-specific alterations as opposed to the wild-type version of the gene or protein, our reagents would be a unique in the IMAT and EDRN armamentaria.

- *Improved Characterization and Verification of Molecular Signatures*: The Strategic Partnering to Evaluate Cancer Signatures (SPEC) Program aims to assemble molecular signature data on several types of cancer. Additionally, a proposed NCI Signature Initiative on chemical genetics for probe and drug development that incorporates molecular characterization centers would also benefit from the resources developed by this project. The NCI Characterization Center would be able to utilize the genomic and proteomics reagents developed in the proposed concept. With TCGA expanding to 20-25 different tumors beginning in FY09, TCGA offers a robust, far-reaching dataset that can augment the molecular signature information being collected by these programs. The project described in this proposal would then specifically generate assays and reagents identified from the molecular data and then provide validation of the target as a valuable component of a specific cancer's molecular signature.

- *Development of Predictive Models of Cancer*: The Integrative Cancer Biology Program (ICBP) represents a multi-disciplinary approach to cancer research. ICBP aims to develop predictive computational and mathematical models. These models would be strengthened by the downstream functional assays that would be enabled by the reagents and assays developed through the proposed initiative. Such data would improve and deepen the *in silico* cancer models developed by ICBP.

In short, this proposal describes an approach that is complementary and non-overlapping with existing programs at the NCI primarily because this project will focus on generating multiplex assays and reagents aimed at specific cancer-associated genomic and epigenomic targets. Moreover, this proposal describes a trans-programmatic pilot study that addresses a major unmet need in translational research and it provides a model for

how to generate resources that can glean the biologically relevant targets from systematic, comprehensive genomic analyses. It is by bridging data from studies like TCGA and TARGET with these resources that can more effectively assess biological and potentially clinical relevance that we can fully bring to bear the power and rigor of genomic-level cancer data. This project would stand alone in this manner.

Justification of Funding Mechanism:

A service contract mechanism (RFP) is preferred over other funding mechanisms. A key deliverable to this pilot involves making the reagents and accompanying data freely available to the scientific community. In the case of proteomic reagents, this is particularly important not just for the mAbs produced, but also for the hybridomas generated and the accompanying data. A service contract mechanism (RFP) is optimal as it allows the government to retain intellectual property (IP) rights to the products, while allowing distributing to the research community at minimal cost through NCI's existing Antibody Characterization Program at NCI-Frederick.

Budget:

Program Activity	Mechanism	Est. # Awards	Total Cost Request
RFP1: Nucleic Acid Reagents and Assays	RFP	2-4 total	$2,500,000
RFP2: Protein-Based Reagents	RFP	2-3 total	$2,500,000
		Total:	**$5,000,000**

Total funding period: 2 years

Evaluation Criteria for RFP(s):

The project will:

- Explore a set number of targets/features for reagent and assay development that can be justified within the budgetary scope of this concept. The selection of targets will be a joint effort with the designated NCI program offices to ensure target overlap between the genomics and proteomics components of this proposal.

- Provide reagents that are targeted against genomic alterations resulting in expression of a unique protein (or peptide) that distinguishes cancer versus normal to the cancer research community. These unprecedented reagents and assays will enable future investigator-initiated proteomics research.

The above evaluation criteria will help determine the next steps for the program. Dependent on outcomes of the pilot program, several options would be considered for next steps, including:

increasing the number of targets/features for reagents development; and inclusion of a broader scope of reagent characterization..

References:

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3. Mutation-Specific Antibodies for the Detection of EGFR Mutations in Non–Small-Cell Lung Cancer. *Clin Cancer Res* OF1 2009;15(9) May 1, 2009.
4. Ludwig, J.A. & Weinstein, J.N., Biomarkers in cancer staging, prognosis and treatment selection. *Nat Rev Cancer* 5 (11), 845-856 (2005).

APPENDIX M

ACRONYMS

FREQUENTLY USED NCI ACRONYMS

ACRIN	American College of Radiology Imaging Network
ACSR	AIDS and Cancer Specimen Resource
ACTNOW	Accelerating Clinical Trials of Novel Oncologic Pathways
AdEERS	Adverse Event Expedited Reporting System
AER	Accelerated Executive Review
AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired Immune Deficiency Syndrome
ARC	Administrative Resource Center
AREA	Academic Research Enhancement Award
ARRA	American Recovery and Reinvestment Act
ASSIST	American Stop Smoking Intervention Study
ATC	Advanced Technology Radiation Therapy Clinical Trials Support
BAA	Broad Agency Agreement
BCERC	Breast Cancer and the Environment Research Centers
BCSC	Breast Cancer Surveillance Consortium
BMTCTN	Blood and Marrow Transplant Clinical Trials Network
BRDPI	Biomedical Research and Development Price Index
BSA	Board of Scientific Advisors
BSC	Board of Scientific Counselors
caBIG	Cancer Bioinformatics Grid
caHUB	Cancer Human Biobank
caIMAGE	Cancer Image database
CAN	Common Account Number
CanCORS	Cancer Care Outcomes Research and Surveillance Consortium
CanQual	Cancer Quality of Care Measures Project
CARRA	Consumer Advocates in Research and Related Activities
CBER	Center for Biologics Evaluation and Research, FDA
CC	Cancer Center
CC	Clinical Center
CCCT	Coordinating Center for Clinical Trials
CCG	Center for Cancer Genomics
CCGs	Clinical Cooperative Groups
CCNE	Center of Cancer Nanotechnology Excellence
CCOP	Community Clinical Oncology Program
CCR	Center for Cancer Research
CCSG	Cancer Center Support Grant
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research, FDA
CDEs	Common Data Elements
CDRP	Cancer Disparities Research Partnership Program
CECCR	Centers of Excellence in Cancer Communication Research
CEPs	Concept Evaluation Panels
CER	Comparative Effectiveness Research
CFR	Code of Federal Regulations
CGs	Cooperative Groups
CGAP	Cancer Genome Anatomy Project
CGCR	Center for Global Cancer Research
CGEMS	Cancer Genetic Markers of Susceptibility
CGN	Cancer Genetics Network
CHP	Consumer Health Profiles
CHTN	Cooperative Human Tissue Network
CIBMTR	Center for International Blood and Marrow Transplant Research
CIRB	Central Institutional Review Board
CIS	Cancer Information Service

CISNET	Cancer Intervention and Surveillance Modeling Network
CIT	Center for Information Technology
CLIA/CAP	Clinical Laboratory Improvement Act and College of American Pathology
CMO	Committee Management Office
CMS	Centers for Medicare and Medicaid Services
CNP	Community Networks Program
CNPP	Cancer Nanotechnology Platforms Partnerships
COI	Conflict of Interest
COMMIT	Community Intervention Trial for Smoking Cessation
Coop. Agr.	Cooperative Agreement
CPTC	Clinical Proteomic Technologies for Cancer
CPTI	Clinical Proteomics Technologies Initiative
CRADA	Cooperative Research and Development Agreement
CRISP	Computer Retrieval of Information on Scientific Programs
CRN	Cancer Research Network
CRP	Cancer Research Portfolio
CRTA	Cancer Research Training Award
CSO	Common Scientific Outline
CSR	Center for Scientific Review
CT	spiral Computed Tomography
CTAC	Clinical and Translational Research Advisory Committee
CTOC	Clinical and Translational Research Operations Committee
CTSU	Clinical Trials Support Unit
CURE	Continuing Umbrella of Research Experiences
DARPA	Defense Advanced Research Projects Agency
DCIDE	Development of Clinical Imaging Drug Enhancers
DCLG	Director's Consumer Liaison Group
DFO	Designated Federal Official
DHHS	Department of Health and Human Services (now HHS)
DOD	Department of Defense
DOE	Department of Energy
DPCPSI	Division of Program Coordination, Planning, and Strategic Initiatives
DSMB	Data and Safety Monitoring Board
eCIS	online Cancer Information Service
EDRN	Early Detection/Diagnosis Research Network
EEO	Equal Employment Opportunity
ER	Extramural Research
ERA	Electronic Research Administration
ERP	Extramural Research Program
ESA	Extramural Support Assistance
EXEC SEC	Executive Secretary
F&A	Facilities and Administration
FACA	Federal Advisory Committee Act
FAR	Federal Acquisition Regulations
FDA	Food and Drug Administration
FDP	Federal Demonstration Partnership
FOA	Funding Opportunity Announcement
FOIA	Freedom of Information Act
FR	*Federal Register*
FTE	Full-Time Equivalent
FTTA	Federal Technology Transfer Act
FUS	Focused Ultrasound
FY	Fiscal Year
GAO	Government Accountability Office
GEI	Genes and Environment Initiative
GIS	Geographic Information System
GMO	Grants Management Officer
GPRA	Government Performance Review Act
GSA	General Services Administration
GWAS	Genome Wide Association Studies
HBCU	Historically Black Colleges and Universities
HCFA	Health Care Financing Administration
HHMI	Howard Hughes Medical Institute
HHS	Department of Health and Human Services (replaces DHHS)
HINTS	Health Information National Trends Survey

HIPAA	Health Insurance Portability and Accountability Act
HMO	Health Maintenance Organization
HSA	Health Scientist Administrator
IACUC	Institutional Animal Care and Use Committee
IARC	International Agency for Research on Cancer
IC	Institute or Center
IC CMO	Institute/Center Committee Management Office(r)
ICBPs	Integrative Cancer Biology Programs
ICMIC	*In Vivo* Cellular and Molecular Imaging Centers
IDSC	Investigational Drug Steering Committee (CCCT)
IHS	Indian Health Service
IISAG	Institute Information Systems Advisory Group
IMAT	Innovative Molecular Analysis Technologies
IND	Investigational New Drug
IOM	Institute of Medicine
IPA	Intergovernmental Personnel Act
IPR	Intellectual Property Rights
IR	Intramural Research
IRB	Institutional Review Board
IRG	Initial/Institutional Review Group
ITGs	Informatics Technology Groups
MARC	Minority Access to Research Careers (NIH)
MBCCOP	Minority-Based Community Clinical Oncology Program
MBRS	Minority Biomedical Research Support Program
mCGAP	Mouse Cancer Genome Anatomy Project
MEO	Most Efficient Organization
MERIT	Method to Extend Research in Time Award (NIH, R37)
MICCP	Minority Institutions Cancer Center Partnerships
MMHCC	Mouse Models of Human Cancer Consortium
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
MTDD	Molecular Target Drug Discovery
MTL	Molecular Targets Laboratory
NAC	National Advisory Council
NASA	National Aeronautics and Space Administration
NBN	National Bio-specimen Network
NCAB	National Cancer Advisory Board
NCBI	National Cancer for Biotechnology Information
NCCCP	NCI Community Cancer Centers Program
NCDDGs	National Cooperative Drug Discovery Groups
NCL	Nanotechnology Characterization Laboratory
NCPB	National Cancer Policy Board
ND	Not discussed
NEJM	*New England Journal of Medicine*
NGA	Notice of Grant Award
NHIS	National Health Interview Survey
NIH	National Institutes of Health
NIH GUIDE	NIH Guide for Grants and Contracts (weekly Web publication)
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
NLST	National Lung Screening Trial
NQF	National Quality Forum
NRFC	Not Recommended for Further Consideration
NRSA	National Research Service Award
NSF	National Science Foundation
NTROI	Network for Translational Research: Optical Imaging
OBC	Operations and Biostatistics Center
OBSSR	Office of Behavioral and Social Science Research
OD	Office of the Director
OEP	Office of Extramural Policy
OER	Office of Extramural Research (NIH)
OFACP	Office of Federal Advisory Committee Policy (formerly NIH/CMO)

OGE	Office of Government Ethics
OHRP	Office for Human Research Protections
OIG	Office of the Inspector General
OLAW	Office of Laboratory Animal Welfare
OMB	Office of Management and Budget
OPERA	Office of Policy for Extramural Research Administration
OPM	Office of Personnel Management
OPRR	Office for Protection from Research Risks (Now OHRP)
ORI	Office of Research Integrity
ORMH	Office of Research on Minority Health (NIH)
ORWH	Office of Research on Women's Health (NIH)
OSTP	Office of Science and Technology Policy
PA	Program Announcement
PAC	Program Advisory Committee
PACCT	Program for the Assessment of Clinical Cancer Tests
PAR	Program Announcement Reviewed/ Receipt
PAS	Program Announcement with Set-aside funds
PBTC	Pediatric Brain Tumor Consortium
PCP	President's Cancer Panel
PCPT	Prostate Cancer Prevention Trial
PCOS	Prostate Cancer Outcomes Study
PD	Program Director/Project Director
PDQ	Physicians Data Query
PET	Positron Emission Tomography
PHS	Public Health Service
PI	Principal Investigator
PLANET	Plan Link Act with Evidence-based Tools
PLCO	Prostate, Lung, Colorectal, and Ovarian
PMA	Premarket Application
PNRP	Patient Navigation Research Network
PO	Program Official
POR	Patient Oriented Research
PRG	Program Review Group
PRG	Progress Review Group
PRODD	Pilot Research to Overcome the Digital Divide
PROG	Peer Review Oversight Group
PROMIS	Patient-Reported Outcomes Measurement Information System
PSA	Physician Scientist Award
QCCC	Quality Cancer Care Committee
QOC	Quality of Care
QOL	Quality of Life
R&R	Research and Related
RAC	Recombinant Activities Committee
RAID	Rapid Access to Intervention Development
RAND	Rapid Access to NCI Discovery
RAPID	Rapid Access to Preventive Intervention Development
RCDC	Research Condition and Disease Categorization
RCMI	Research Centers in Minority Institutions
RFA	Request for Application (Grants)
RFP	Request for Proposal (Contracts)
RM	Roadmap
RPG	Research Project Grant
RWJ	Robert Wood Johnson Foundation
SAMHSA	Substance Abuse and Mental Health Services Administration
SBIR	Small Business Innovation Research
SEER	Surveillance, Epidemiology, and End Results
SEP	Special Emphasis Panel
SGE	Special Government Employee
SNAP	Streamlined Noncompeting Award Process
SoC	Standards of Conduct
SOW	Statement of Work
SPIN	Shared Pathology Informatics Network spiral
SPL	Scientific Program Leadership
SPNs	Special Population Networks
SPORE	Specialized Program of Research Excellence
SREA	Scientific Review Evaluation Award
SRG	Scientific Review Group

SRO	Scientific Review Officer
SSS	Special Study Section
STTR	Small Business Technology Transfer
TARGET	Theapeutically Applicable Research to Generate Effective Treatments
TARP	Tissue Array Research Program
TCGA	The Cancer Genome Atlas
TREC	Transdisciplinary Research on Energetics and Cancer
TRIO	Translating Research Into Improved Outcomes
TRWG	Translational Research Working Group
TTURCs	Transdisciplinary Tobacco Use Research Centers
VA	Veterans Administration

NCI ORGANIZATIONAL ACRONYMS

Division/Center(s):

DCB	Division of Cancer Biology
DCCPS	Division of Cancer Control and Population Sciences
DCEG	Division of Cancer Etiology and Genetics
DCP	Division of Cancer Prevention
DCTD	Division of Cancer Treatment and Diagnosis
DEA	Division of Extramural Activities
CCP	Cancer Centers Program
CCR	Center for Cancer Research
CCT	Center for Cancer Training
CRCHD	Center to Reduce Cancer Health Disparities
CSSI	Center for Strategic Scientific Initiatives
FCRDC	Frederick Cancer Research & Development Center
NCICB	Center for Bioinformatics
TTC	Technology Transfer Center
SBIRDC	Small Business Innovative Research Development Center

Programs/Offices/Branches:

ACRB	Applied Cancer Screening Research Branch
AERB	Analytic Epidemiology Research Branch
AISB	Applied Information Systems Branch
AO	Administration Operations
ARC	Administrative Resource Centers
ARP	Applied Research Program
BBRB	Basic BioBehavioral Research Branch
BGCRG	Breast and Gynecologic Cancer Research Group
BIP	Biomedical Imaging Program
BOD	Business Operations and Development
BPSRG	Basic Prevention Science Research Group
BR	Biological Resources
BRB	Biometric Research Branch
BRB	Biological Resources Branch
BRB OC	Biological Resources Branch Oversight Committee
BRP	Behavioral Research Program
CADRG	Chemopreventive Agent Development Research Group
CBIIT	Center for Biomedical Informatics and Information Technology
CBRG	Cancer Biomarkers Research Group
CCB	Cancer Centers Branch
CCBB	Cancer Cell Biology Branch
CCP	Cancer Centers Program
CDP	Cancer Diagnosis Program
CEB	Cancer Etiology Branch
cGAP	Cancer Genome Atlas Project Office
CGCB	Clinical Grants and Contracts Branch
CIB	Clinical Investigations Branch
CIHB	Cancer Immunology and Hematology Branch
CIP	Cancer Imaging Program
CIS	Office of Cancer Information Service
CMBB	Comprehensive Minority Biomedical Branch
COPTRG	Community Oncology and Prevention Trials Research Group
CROB	Clinical Radiation Oncology Branch

CSB	Cancer Statistics Branch
CSSI	Center for Strategic Scientific Initiatives
CTB	Cancer Training Branch
CTCP	Clinical Proteomic Technologies for Cancer
CTEB	Clinical and Translational Epidemiology Branch
CTEP	Cancer Therapy Evaluation Program
DCAB	DNA and Chromosome Aberrations Branch
DIB	Diagnostic Imaging Branch
DRB	Diagnostics Research Branch
DRB	Disparities Research Branch
DTP	Development Therapeutics Program
EDRG	Early Detection Research Group
EFDB	Extramural Financial Data Branch (Now OEFIA)
EGRP	Epidemiology and Genetics Research Program
EO	Ethics Office
FMOSB	Frederick Management Operations and Support Branch
GCOB	Grants and Contracts Operations Branch
GOCRG	Gastrointestinal and Other Cancer Research Group
HCIRB	Health Communications and Informatics Research Branch
HPB	Health Policy Branch
HPRB	Health Promotion Research Branch
HRMCB	Human Resources Management and Consulting Branch
HSEB	Health Services and Economics Branch
HSFB	Host Susceptibility Factors Branch
IDB	Investigational Drug Branch
IGIB	Image Guided Intervention Branch
IRO	Institute Review Office
ISCS	Information Systems and Computer Services
ISTB	Information Systems Technology Branch
ISWG	Imaging Sciences Working Group
ITDB	Imaging Technology Development Branch
LUACRG	Lung and Upper Aerodigestive Cancer Research Group
MAB	Management Analysis Branch
MFRB	Modifiable Risk Factors Branch
MIB	Molecular Imaging Branch
MRTB	Molecular Radiation Therapeutics Branch
MTB	Method and Technologies Branch
NSRG	Nutritional Science Research Group
OA	Office of Acquisitions
OAR	Office of Advocacy Relations
OBBR	Office of Biorepositories and Biospecimens Research
OBF	Office of Budget and Finance
OCCAM	Office of Cancer Complementary and Alternative Medicine
OCE	Office of Communications and Education
OCG	Office of Cancer Genomics
OCNR	Office of Cancer Nanotechnology Research
OCRP	Office of Clinical Research Promotion
OCS	Office of Cancer Survivorship
OCTR	Office of Centers, Training and Resources
OD	Office of the Director
OEA	Office of Extramural Applications
OEFIA	Office of Extramural Finance and Information Analysis (formerly EFDB)
OESI	Office of Education and Special Initiatives
OGA	Office of Grants Administration (formerly GAB)
OGCR	Office of Government and Congressional Relations
OHAM	Office of HIV and AIDS Malignancy
OIA	Office of International Affairs
OLACPD	Office of Latin American Cancer Program Development
OM	Office of Management
OPSO	Office of Physical Sciences-Oncology

ORB	Outcomes Research Branch
ORRPC	Office of Referral Review and Program Coordination
OSCB	Organ Systems Coordinating Branch
OSPA	Office of Science Planning and Assessment
OTIR	Office of Technology and Industrial Relations
OWH	Office of Women's Health
PCRB	Program Coordination and Referral Branch
PUCRG	Prostate and Urologic Cancer Research Group
RAEB	Research Analysis and Evaluation Branch
RCAB	Research Contracts and Acquisition Branch
RDB	Resources Development Branch
RDB	Radiotherapy Development Branch
REB	Radiation Effects Branch
RFMMB	Risk Factor Monitoring and Methods Branch
RPRB	Research Programs Review Branch
RRP	Radiation Research Program
RTRB	Resources and Training Review Branch
SBMAB	Structural Biology and Molecular Applications Branch
SPL	Scientific Program Leadership
SRAB	Statistical Research Application Branch
SRLB	Special Review and Logistics Branch
SRP	Surveillance Research Program
STRIIC	Strategic Technical Review and Innovative Initiative Core
TBMB	Tumor Biology and Metastasis Branch
TCRB	Tobacco Control Research Branch
TDB	Technology Development Branch
TDCB	Technology Development and Commercialization Branch
TRP	Translational Research Program

NIH ORGANIZATIONAL ACRONYMS

CC	Clinical Center
CIT	Center for Information Technology
CSR	Center for Scientific Review (formerly Division of Research Grants)
FIC	John E. Fogarty International Center
FNIH	Foundation for the National Institutes of Health
NCCAM	National Center for Complementary and Alternative Medicine
NCI	National Cancer Institute
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/ Biotechnology
NICHD	National Institute of Child Health and Human Development
NIDA	National Institute on Drug Abuse
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIDR	National Institute of Dental and Craniofacial Research
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
NIMHD	National Institute on Minority Health and Health Disparities
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute for Nursing Research

APPENDIX N

CLINICAL RESEARCH AND CLINICAL TRIALS

Clinical Research: NIH defines human clinical research as: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research. *Note*: Not considered clinical research by this definition is: research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Clinical Trial: For purposes of reviewing applications submitted to the NIH, a clinical trial is operationally defined as a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Clinical trials of experimental drug, treatment, device, or behavioral intervention may proceed through the following phases:

- **Phase 0** trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer.

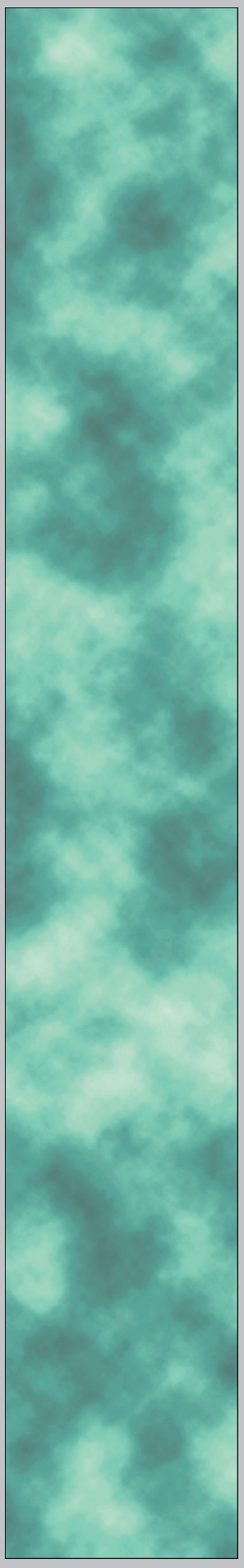
- **Phase I** clinical trials are conducted to test a new biomedical or behavioral intervention in a small group of people (e.g., 20-80) for the first time to evaluate safety (e.g., determine a safe dosage range, and identify side effects).

- **Phase II** clinical trials are done to study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety.

- **Phase III** studies are conducted to study the efficacy of the biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the interventions to be used safely.

- **Phase IV** studies are done after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

NIH-Defined Phase III Clinical Trial: For the purpose of the NIH Grants Policy Guidelines, an NIH-defined Phase III clinical trial is a broadly based prospective NIH-defined Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments. Often, the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials also are included. ***For more information, please visit:*** http://www.cancer.gov/cancertopics/factsheet/information/clinical-trials/**.**



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