Final FY 2003 GPRA Annual Performance Plan, Revised Final FY 2002 GPRA Annual Performance Plan, and FY 2001 GPRA Annual Performance Report

U.S. Department of Health and Human Services

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National Institutes of Health
Government Performance and Results Act
Final FY 2003 GPRA Annual Performance Plan, Revised Final FY 2002 GPRA Annual Performance Plan, and FY 2001 GPRA Annual Performance Report

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Introduction

In 1993, Congress passed and the President signed into law the Government Performance and Results Act (GPRA), P.L. 103-62. This legislation's broad intent is to enhance the effectiveness, efficiency, and accountability of government programs by directing federal agencies to more sharply focus their management efforts on the results that program spending yields. With better information on spending and program effectiveness, federal managers are expected to be better able to improve program performance. GPRA is also expected to make information on program performance more readily available to the Congress for policymaking, spending decisions, and program oversight.

Consistent with the Department of Human Health and Service's (DHHS) approach, this document integrates the National Institute of Health's (NIH) Annual Plan and Annual Report into a single document to eliminate redundancy and to facilitate presentation of the overall thrust of the agency's program strategies and accomplishments across multiple years. NIH's FY 2003 performance plan represents the culmination of lessons learned from previous GPRA performance plans and reports. It provides a picture of NIH's key activities, strategies, and performance goals undertaken to accomplish NIH's mission.

The planning elements of this document describe NIH's mission and long term goals; the resources available; and the programs, strategies, and performance expectations that mark the agency's intended path toward achieving these goals. The goals and targets described for FY 2003 are "initial" and FY 2002 are "revised final." The document also includes previously published "revised final" FY 2001 goals and targets.

The reporting elements of this document describe NIH's accomplishments and progress toward goal achievement during FY 1999 - FY 2001.

The Office of Evaluation, Office of Science Policy in NIH's Office of the Director prepared this document. If you have questions or comments, please contact John Uzzell, Director, Office of Evaluation on (301) 496-9285.

An electronic version of this document will be available in March 2002 from NIH's World Wide Web server at the following address: http://www1.od.nih.gov/gpra/default.htm. Previous performance plans and reports are available now.

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Executive Summary

Founded in 1887, the National Institutes of Health (NIH) is the federal focal point for medical research in the United States. Composed of 27 separate Institutes and Centers, NIH is one of eight health agencies of the Public Health Service, a major component of the U.S. Department of Health and Human Services (DHHS). NIH's mission is to uncover new knowledge about the prevention, detection, diagnosis, and treatment of disease and disability, from the rarest genetic disorder to the common cold.

The FY 2003 Annual Performance Plan and FY 2002 Annual Performance Plan serve to help NIH pursue its mission, highlighting goals that are used to track its performance. The FY 2001 Annual Performance Report presents 41 goals that had active targets for FY 2001. Due to the cross-cutting nature of disease and scientific discovery, NIH has organized its performance goals under three Core GPRA Programs:

- Research Program
- Research Training and Career Development Program
- Research Facilities Program

The 27 performance goals of the *Research Program* focus on enhancing research outcomes across the medical research continuum by supporting research in NIH's own intramural laboratories as well as the research of non-federal scientists working in universities, medical schools, hospitals, and research institutions throughout the country. Through its Research Program, NIH also focuses on communicating scientific results, promoting the efficient transfer of new drugs and other technologies, and providing effective research leadership and administration.

The six goals for the *Research Training and Career Development Program* support research training and outreach designed to ensure a continuing supply of well-trained scientists. The eight goals for the *Research Facilities Program* focus on modernizing and improving intramural and extramural research facilities to ensure that the nation's scientists have adequate facilities in which to conduct their work.

Research Program

NIH's Research Program addresses its long-term goals "to increase understanding of normal and abnormal biological functions and behavior" and "to improve prevention, diagnosis, and treatment of diseases and disabilities." NIH organizes performance goals for this Core Program under four functional areas: (1) Research Outcomes, (2) Communication of Results, (3) Technology Transfer, and (4) Research Leadership and Administration.

Research Outcomes. NIH strives to improve prevention and treatment of human disorders by maximizing support for basic biomedical research, promoting health, and better understanding the biological and behavioral basis for disease. NIH reported on seven Research Outcomes performance goals that demonstrated NIH's primary focus to produce research results that directly supported its mission in FY 2001. For FY 2002, the goal structure was modified as NIH combined two closely related goals and added two subgoals each to four of the goals.

- Add to the body of knowledge about normal and abnormal biological functions and behavior.

  Subgoals

  a1) Discover innovative approaches for identifying and measuring genetic and environmental factors that contribute to common, complex diseases across populations.

  a2) Develop model systems (animal models, cell lines, etc.) that will advance our understanding of disease processes.

- Develop new or improved instruments and technologies for use in research and medicine.

  Subgoals

  b1) Develop new technologies to enable greater understanding of genomic and proteomic information.

  b2) Develop biocompatible materials for use in replacing or repairing damaged and non-functioning or missing tissue.

- Develop new or improved approaches for preventing or delaying the onset or progression of disease and disability.

  Subgoals

  c1) Identify modifiable risk factors for disease/disability.

  c2) Identify, develop, and test new/improved medications for the prevention of disease/disability.

- Develop new or improved methods for diagnosing and treating disease and disability.[1]

  Subgoals

  d1) Develop and apply powerful new imaging, genetic, and biological technologies to enable early and more precise diagnosis and intervention.

  d2) Identify and apply knowledge about factors, including gender, race, ethnicity, and socioeconomic status, to improve diagnostic reliability and treatment response.

- Develop new or improved methods for diagnosing disease and disability.[2]

- Develop new or improved methods for treating disease and disability.[2]

- Develop critical genomic resources, including the DNA sequences of the human genome and the genomes of important model organisms and disease-causing microorganisms.

- Develop an AIDS vaccine by 2007.

Communication of Results. Communicating scientific results and health information to the medical research community, health care providers, patients, and the public has long been recognized as a critical NIH function. Currently, NIH has five performance goals that focus on communicating the results of NIH supported research:

- Increase awareness of NIH-sponsored research among health care providers to promote research application.

- Increase awareness of NIH-sponsored research results among racial/ethnic minorities and high risk, underserved, and/or affected publics.

- Increase awareness of NIH-sponsored research results among the general public.

- Increase awareness of clinical research and support participation in clinical trials.

- Establish a Clinical Trials Database, as required by the FDA Modernization Act.

[1] In FY 2002 two previously listed goals, "Develop new or improved methods for diagnosing disease and disability," and "Develop new or improved methods for treating disease and disability" were combined to create this goal.

[2] These two goals are reported on separately in FY 2001, but combined and supplemented with subgoals for FY 2002 and beyond (see previous footnote).

Technology Transfer. NIH facilitates development of new drugs and other products to benefit human health by promoting efficient transfer to the private sector of new technology forthcoming from NIH research. In addition to improving public health, technology transfer contributes to the global competitiveness of the nation's businesses and to the nation's economic prosperity. NIH has three performance goals that seek to enhance its technology transfer activities:

- Increase the number of scientists who have received training in technology transfer.
- Develop a system to identify and measure the health outcomes of technologies licensed by NIH.
- Maintain oversight and protection of the public investment in NIH research through increased monitoring of licensee activities.

*Research Leadership and Administration***.** All of the NIH ICs are actively involved in research leadership and administration, which requires effective coordination of priority setting, grants administration and peer review, and agency management and administrative support. NIH has established 12 performance goals related to the challenges of 1) ensuring that NIH research is responsive to emerging public health needs, scientific opportunities, and new technologies; 2) maintaining effective and efficient processes for reviewing, selecting, and administering extramural research grants; and, 3) maintaining effective internal management systems and providing strong administrative support to the research community:

- Ensure that NIH-supported research reflects the changing nature of scientific opportunities and public health needs.
- Improve electronic Research Administration (eRA) technology by developing capability for end-to-end electronic research administration by 2004.
- Ensure proper stewardship of public funding for research.
- Ensure that the NIH peer review process keeps pace with current advances in research and that the expertise of peer reviewers is appropriate for the needs of modern science.
- Develop innovative business practices to facilitate government/public interactions.
- Improve grantee reporting of inventions developed with federal funds.
- Implement the recommendations of the Arthur Andersen, Inc. study of administrative practices and costs at NIH.
- Improve the efficiency of the small acquisition process by continuing to expand the Purchase Card Program.

- Expand the use of Performance Based Contracting (PBC).

- Identify and pilot new approaches to providing human resource services which increase manager satisfaction with personnel system flexibility and ease of use.

- Recruit and retain highly qualified extramural investigators to biomedical/ behavioral research through the use of student loan repayment programs.

- Implement government-wide initiative on delayering management levels and streamlining organization.

Research Training and Career Development Program

NIH's Research Training and Career Development Program addresses its long-term goal to "promote development of a talent base of well qualified, highly trained, and diverse investigators capable of yielding the scientific discoveries of the future." NIH's performance goals for this Core Program are organized under one functional area: Training Support and Outreach. NIH has six performance goals that demonstrate NIH's efforts to enhance training programs at the predoctoral, postdoctoral, and early career developmental levels. These goals ensure a continuing supply of capable individuals in areas of national need, encourage participants to pursue research careers, and foster the recruitment and retention of underrepresented groups into careers as researchers:

- Respond to the National Academy of Sciences quadrennial report on the future needs for health-related researchers.

- Maintain adequate application and award rates in key training support areas.

- Increase the pool of clinician researchers trained to conduct patient-oriented research.

- Increase the participation of underrepresented racial and ethnic groups, women, and individuals with disabilities in NIH training and research programs.

- Expand capabilities for electronic administration of research training and career development activities.

- Improve the capabilities for career outcome tracking for NIH training and career development programs.

Research Facilities Program

NIH's Research Facilities Program addresses its long-term goal to "secure facilities for research that are modern, efficient, and safe." NIH's eight performance goals for this Core Program are

organized under two functional areas: (1) Intramural Modernization and Improvements, and (2) Extramural Assistance.

Intramural Modernization and Improvements. NIH has seven performance goals that demonstrate NIH efforts to construct, renovate, and maintain NIH research facilities located on the Bethesda campus and at off-campus field stations to enable NIH intramural researchers to continue to conduct state-of-the-art medical research:

- Improve the operating conditions and environment of intramural facilities and the availability and reliability of NIH utility distribution systems to support intramural research.
- Complete the Louis Stokes Laboratories Building.
- Complete the Mark O. Hatfield Clinical Research Center.
- Complete the Warren Grant Magnuson Clinical Center Revitalization Program.
- Maintain the quality of the NIH Animal Care Program and construct a Central Vivarium.
- Complete the John Edward Porter Neuroscience Research Center on the NIH Bethesda Campus
- Establish a systematic process to manage and account for NIH's Real Property Inventory.

Extramural Assistance. NIH has one performance goal that focuses on key NIH extramural assistance activities related to the construction and modernization of non-federal facilities at academic institutions and other centers of research excellence to enhance their ability to initiate and continue to conduct high-quality research:

- Approve an optimal percent of construction designs by the end of the third year that are in compliance with federal and NIH design regulations and guidelines, and with other relevant local, national, and international codes and standards.

Part I
Agency Context for Performance Measurement

1.1 NIH Mission and Long Term Goals

The NIH mission is to uncover new knowledge about the prevention, detection, diagnosis, and treatment of disease and disability.

NIH works toward this mission by conducting research in its own laboratories; supporting the research of non-federal scientists in universities, medical centers, hospitals, and research institutions throughout the country and abroad; helping to train research investigators; and fostering communication of medical information.

Medical innovation is one of the principal foundations on which America's past successes in improving healthcare have been built. It is where hope for the future resides. History provides abundant evidence that medical progress rarely occurs without the sustained pursuit of advances in basic and behavioral science. Through the conduct and support of medical research, NIH seeks to expand fundamental knowledge about the nature and behavior of living systems; to improve and develop new strategies for the diagnosis, treatment, and prevention of disease; and to reduce the burdens of disease and disability.

NIH invests the public's resources and support for medical science in three basic and interrelated ways. First and foremost, NIH conducts and supports medical research. Second, it contributes to the development and training of the pool of scientific talent. And third, it participates in the support, construction, and maintenance of the laboratory facilities necessary for conducting cutting-edge research.

NIH's long-term goals encompass each of these important domains of agency activity:

- ***Increase understanding of normal and abnormal biological functions and behavior.***
- ***Improve prevention, diagnosis, and treatment of diseases and disabilities.***
- ***Promote development of a talent base of well qualified, highly trained, and diverse investigators capable of yielding the scientific discoveries of the future.***
- ***Secure facilities for research that are modern, efficient, and safe.***

The agency's activities and strategies discussed throughout this plan are directed at realizing all of these overarching goals.

1.2 Organization, Programs, Operations, Strategies, and Resources

Organizational Overview

NIH is comprised of twenty-seven Institutes and Centers (ICs, or "Institutes") whose research activities extend from basic research that explores the fundamental workings of biological systems and behavior, to studies that examine disease and treatments in clinical settings, to prevention and to population-based analyses of health status and needs. (A brief mission statement for each of the Institutes appears in Appendix 5.)

The NIH "visible" to most Americans encompasses the research institutes focused on diseases (e.g., cancer, diabetes), primary organ systems (e.g., heart, eye, kidney), or a stage of life (e.g., children, the aging). Yet, no less essential to the nation's health are NIH programs that address overarching scientific needs and opportunities. Included here are such efforts as deciphering the human genome, understanding cellular and tissue biology and physiology, training investigators in relevant scientific fields, and developing the array of technologies dictated by the needs of cutting-edge research. All are scientific innovations that move into clinical practice and enhance the capabilities and quality of routine medical treatment.

The Extramural Research Community. More than $8 out of every $10 dollars appropriated to NIH flows out to the scientific community at large -- of which the lion's share supports individual scientists. This "extramural" system is premised on *independence*, embodied in "investigator- initiated" research; on *self-governance*, embodied in peer review of scientists by scientists as the primary basis for judging the merits of research proposals and awarding funds; and on the powerful incentive of *competition* among the most highly trained scientists in the world. The extramural research community numbers an estimated 50,000 scientists affiliated with some 2,000 university, hospital, and other research facilities located in all 50 states, the District of Columbia, Puerto Rico, Guam, the Virgin Islands, and points abroad.

Research at NIH's Intramural Laboratories. A much smaller fraction of the funds -- approximately 9 percent of the budget -- supports a core program of basic and clinical research activities administered and staffed by NIH's own physicians and scientists. This in-house, or intramural, research program includes the NIH Clinical Center and other resources that provide scientific, clinical, and educational benefits to the citizens of the U.S. and the world.

GPRA Programs

For purposes of planning and performance assessment under GPRA, NIH organizes its main activities into three Core Programs: 1) Research, 2) Research *Training and Career Development*, and 3) *Research Facilities*.

The ***Research Program*** represents all aspects of the medical research continuum, including basic research, which may be disease-oriented; observational and population-based research; behavioral research; clinical research, including research to understand both normal health and

disease states, to move laboratory findings into medical applications, to assess new treatments or to compare different treatment approaches; and health services research. In addition, the timely dissemination of medical and scientific information is a key component of the Program, as is the expeditious transfer of the results of its medical research to provide benefits to human health.

The ***Research Training and Career Development Program*** addresses the need for creative and capable personnel to conduct medical research. The primary goal of the support that NIH provides for graduate training and career development is to produce new, highly trained investigators who are likely to perform research that will benefit the nation's health. Our ability to maintain the momentum of recent scientific progress and our international leadership in medical research depends upon the continued development of new, highly trained investigators.

The ***Research Facilities Program*** focuses on ensuring that the scientists we support have adequate facilities in which to conduct their work. In fact, many of the advances in medical research that are leading to more effective treatments for illnesses reflect stunning innovations in sophisticated, but often costly, research technologies that are far beyond the capacity of all but a handful of institutions to purchase, construct, or maintain. NIH recognizes that ensuring broad access to these research resources creates efficiencies that make the research dollar go farther, while providing critical resources to all scientists. Often, access to the needed tools by the largest possible number of scientists determines the pace of research on many devastating illnesses.

Throughout, NIH's Core Programs are aggregates of the many specific programs and activities underway across the agency. This aggregation approach is implemented due to the cross-cutting nature of disease and scientific discovery. By aggregating activities that are intrinsically collaborative and complementary, NIH neither omits nor minimizes the significance of any particular activity that contributes to a major function or operation for the agency as a whole.

Operations and Broad Strategy

NIH's mission to advance medical knowledge and sustain the nation's medical research capacity is accomplished by sustained federal stewardship. It is achieved through a number of fundamental principles that underlie NIH's broad planning and management of its programs and resources. These principles comprise the basic context in which NIH's goal setting and strategic planning operate.

■ ***Provide scientific leadership and establish research priorities.*** Establishing research priorities is essential to ensure that science meets national public health needs and efficiently uses limited resources. NIH uses a multi-level system to establish and review research priorities. The NIH Director, in collaboration with IC directors and their respective advisory councils and boards and the biomedical research community, guides the priority-setting process. Additional input is sought from the Department of Health and Human Services (DHHS), Congress, and the public. Reflecting the research priorities identified through this process, ICs examine research

initiatives and public health needs to ensure that NIH is committing federal resources to projects and programs that will achieve the greatest yield from the nation's medical research investment.

Public health need and scientific opportunity are the primary drivers in the allocation of resources. In general, NIH sponsors research that addresses public health needs – to find ways to prevent, treat, or cure disease and to minimize pain and suffering. But public health need alone is not enough; there must also be some real opportunity for success.

How do we identify areas of increased scientific opportunity? New knowledge comes from the pursuit of answers to new questions. The rate-limiting step in the generation of new knowledge is not the number of experiments conducted, but rather the number of new hypotheses or questions. When an arena of research is enjoying an exponential increase in the number of new questions, it is, indeed, an area of scientific opportunity. New questions emerge as a result of several converging factors, including the creativity of individual investigators, the emergence of new methods and tools that allow previously unanswered questions to be addressed, and what is already known about a problem. It is imperative that NIH capitalize by investing funds in areas of scientific opportunity.

■ ***Fund the best research.*** Research Project Grants (RPGs) are the core mechanism for NIH support for the individual investigator. Other mechanisms include Program Project Grants, which support multi-disciplinary projects conducted by several collaborating investigators, and Center Grants, which are used to fund multi-disciplinary programs of medical research. Scientists working at universities, medical, dental, nursing and pharmacy schools, schools of public health, non-profit research foundations, and private industry submit research proposals to NIH. NIH support for a project includes the salaries of the scientists and technicians; the cost of equipment such as lasers or computers; the cost of supplies such as chemicals and test tubes; the cost of procedures conducted with research subjects; and the indirect costs associated with doing research, such as maintenance of buildings, electricity, library services, and cost of administrative support. Part of the NIH budget is also spent on research and development contracts that are awarded to non-profit and commercial organizations for work requested and overseen by NIH.

NIH funds are awarded through a highly competitive process to the most promising and productive scientists. Extramural research proposals are first evaluated by expert scientific peer review panels composed of non-NIH scientists who are among the most knowledgeable and respected in their fields. The proposals are then reviewed by independent advisory councils that include members of the lay public. This two-tiered independent review system is critical to ensuring that the best research proposals are funded from the more than 40,000 grant applications NIH receives each year.

■ ***Conduct leading-edge research in NIH laboratories.*** NIH also conducts basic and clinical research in its own (intramural) laboratories. Projects are selected on the basis of scientific merit and public health need. Each institute maintains a Board of Scientific Counselors, composed of external experts, that reviews the intramural programs and makes recommendations to the Institute Director. The intramural program enables scientists to apply the results of laboratory

research to patient care and to seek answers in the laboratory to questions that arise in the clinical setting. This national resource permits NIH to respond rapidly to critical health problems and emergencies and to take advantage of emerging opportunities.

■ ***Effectively disseminate scientific results and research-based health information.*** NIH develops and disseminates informational materials to individuals and groups, including medical and scientific organizations, industry, the media, and volunteer and patient organizations. Information dissemination efforts have expedited the translation of NIH's scientific advances and technologies into important diagnostic, preventive, and therapeutic products. In addition, they have brought about major health-enhancing changes in public attitudes and behaviors, such as reduction of smoking and better control of high blood pressure and high cholesterol levels. To effectively reach diverse audiences, whose knowledge of science and health differ, NIH disseminates information ranging from highly technical research advances to the steps individuals can take to improve their own health.

NIH disseminates information on scientific findings and technologies to scientific and other health professionals through various avenues: scientific publications, workshops and symposia, scientific meetings, consensus development conferences, press releases, special physician education programs, and clinical alerts concerning immediate health and safety issues. NIH also provides access to information about scientific articles, NIH research grants, clinical trials and treatment through extensive electronic databases.

To respond to the public, Congress, and the media, NIH employs information offices, clearinghouses, electronic databases, Internet-based information services, public education programs, publications and press releases, as well as direct responses by letter and telephone. These provide information regarding participation in research protocols; the best current information on disease prevention and health promotion, diagnosis, and treatment of specific diseases and disorders; information about ongoing research; and referrals to other sources of information.

■ ***Facilitate the development of health-related products through technology transfer.*** NIH has a statutory mandate to transfer new biomedical technologies to the private sector for further development and commercialization. NIH's technology transfer programs ensure that the public investment in NIH research leads rapidly to beneficial health-related products, including preventives, diagnostics, therapeutics, and vaccines.

Many NIH research results are converted into commercial medical products, typically through the publicly available knowledge base created by NIH-supported research. The public also benefits from NIH technology transfer activities, including Cooperative Research and Development Agreements (CRADAs) with the private sector and the licensing to industry of intellectual property rights arising out of CRADAs and other NIH research. Virtually all NIH licenses negotiated with industry are royalty bearing.

■ ***Ensure a continuing supply of well-trained laboratory and clinical investigators.*** Whereas supporting research is essential, it is equally important to ensure the availability of well-trained

investigators who reflect our nation's diversity and who have specialized knowledge, methodological expertise, and creativity. NIH's research training grant portfolio covers all the career stages that are key to the recruitment, training, and retention of productive medical researchers.

One of the goals of research training is to teach pre- and post-doctoral students how to conduct innovative, high-quality science, including how to identify problems, develop hypotheses, design experiments, choose model systems, and see connections among different fields that allow a scientist to make quantum leaps in understanding a problem. Mentors are a critical training resource, serving as role models and providing guidance that ensures trainees develop into successful investigators.

■ ***Sustain the nation's research facilities.*** NIH must continually support the development, maintenance, and renewal of physical resources that are vital to the rapid pace of scientific discovery. The past achievements of medical research have required access to state-of-the-art laboratories. Up-to-date and safe research facilities are essential to assuring continued progress in the medical sciences. To support intramural research, NIH constructs new facilities and renovates existing ones to meet the ever-changing needs of biomedical research. NIH also provides support to extramural grantees through research facilities construction grants designed to assist in the construction and modernization of non-federal research facilities.

■ ***Collaborate and coordinate with others.*** NIH collaborates and coordinates on an ongoing basis with other federal agencies and research organizations where research interests intersect and when joint efforts will enhance the individual activities of each entity. Medical research benefits from multiple perspectives being brought to bear on a particular problem. Collaborative efforts bring diverse domains of expertise together and can facilitate a more rapid response to emerging opportunities. In addition, collaborative efforts work to produce the best possible science while making the most economical use of the resources available.

These collaborative endeavors frequently involve NIH's sister agencies in DHHS, including the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC) and the Agency for Healthcare Research and Quality (AHRQ). Nonetheless, the full scope of NIH's collaborative activities -- both in the past and those contemplated for the future -- is far wider, including many other federal agencies, government bodies, non-governmental organizations, and industry.

Resources

The FY 2003 President's budget request provides funding to support NIH staff, including approximately 2,000 intramural scientists; research efforts from a pool of extramural scientists; and the facilities necessary to conduct science (i.e., universities, research centers and the buildings on the NIH campus). The combination of dollars, human capital, and physical facilities available for research make up the resources by which NIH accomplishes its program performance goals. Under NIH's aggregated approach, performance goals are grouped under the

three NIH Core Programs: Research, Research Training and Career Development, and Research Facilities. The following table provides a five-year summary of funding for these programs.

	FY 2003 President's Budget Request[1] (dollars in thousands)				
	FY 1999 Actual	**FY 2000 Actual**	**FY 2001 Actual**	**FY 2002 Estimate**	**FY 2003 Request**
Research	$14,580,705	$16,692,719	$19,214,206	$21,932,194	$25,103,261
Research Training and Career Development	811,120	912,241	1,023,475	1,151,485	1,247,741
Research Facilities	239,343	251,747	248,386	458,677	907,999
All Programs	**$15,631,168**	**$17,856,707**	**$20,486,067**	**$23,542,356**	**$27,259,001**

[1] Comparable for the Managerial Flexibility Act of FY 2001.

Although Congress appropriates funds to each IC, the funds are distributed through certain budget mechanisms to support NIH's three core programs. The following is a brief overview of the budget mechanisms used to support each program.

The vast majority of NIH's funding supports the ***Research Program***, which is NIH's highest priority. NIH uses the following nine budget mechanisms to provide funding to this program: Research Project Grants (RPGs), Intramural Research, Research Centers, Research and Development Contracts, Cancer Prevention and Control, Library of Medicine, Other Research (e.g., research careers, cancer education, cooperative clinical research, minority biomedical research support), Research Management and Support (RMS), and Office of the Director (OD). RPGs, the primary source of support, allow NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities.

Through the ***Research Training and Career Development Program***, NIH provides the biomedical research enterprise with a steady flow of highly-trained researchers equipped to conduct the nation's research mission. Although a majority of these funds are provided through the Research Training budget mechanism, funding is also provided through the Other Research, RMS, and OD mechanisms.

NIH provides facilities support for the NIH campus and for universities and research centers through the ***Research Facilities Program***. Primarily, the Buildings and Facilities and Construction budget mechanisms support this program. The RMS and OD budget mechanisms provide additional funding.

The following table identifies the amount of FY 2001 funds provided to each NIH program through its associated budget mechanisms.

Budget Mechanism	FY 2001 Actual[1] (000's)	Program	Program Resources (000's)
Research Project Grants	$ 11,576,415	**Research** • Research • Communication of Results • Technology Transfer • Research Leadership and Administration	$ 19,214,206
Intramural Research	2,014,546		
Research Centers	1,859,389		
Research and Development Contracts	1,371,179		
Cancer Prevention and Control	461,572		
Library of Medicine	242,398		
Other Research[2]	825,938		
Research Management and Support[3]	675,418		
Office of the Director[4]	187,351		
Research Training	$ 589,704	**Research Training and Career Development** • Training Support and Outreach	$ 1,023,475
Other Research[2]	394,581		
Research Management and Support[3]	35,817		
Office of the Director[4]	3,373		
Buildings and Facilities	$ 160,876	**Research Facilities** • Intramural Modernization and Maintenance • Extramural Assistance	$ 248,386
Construction	78,000		
Research Management and Support[3]	8,691		
Office of the Director[4]	819		
All Mechanisms	**$ 20,486,067**	**All Programs**	**$ 20,486,067**

[1] Comparable for the Managerial Flexibility Act of FY 2001.
[2] The Other Research budget mechanism supports both the Research Program and the Research Training and Career Development Program.
[3] The Research Management and Support budget mechanism supports all programs.
[4] The Office of the Director budget mechanism supports all programs.

1.3 Partnerships and Coordination

NIH collaborates with numerous organizations to pursue its longer-term goals in most all of its major program areas. Such partnerships include competitively-funded grants to the universities, medical schools, and other research entities that comprise the Extramural Research Community. There are also joint efforts with other federal agencies, both within DHHS, with other departments, and with private industry.

Where research and related interests intersect and joint efforts can enhance individual activities, the reasons for such collaboration are many. Research benefits from the multiple perspectives and more diverse expertise that can be brought to bear on a particular problem. Collaboration works to produce the best possible science while making more economical use of the resources available. And, importantly, partnering can facilitate more rapid response to emerging opportunities.

Partnership with the Extramural Research Community

Research grants to the Extramural Research Community comprise the main body of NIH research -- and these scientists are NIH's principal "partners" in the overall research enterprise. Currently, this research community numbers an estimated 50,000 scientists, affiliated with some 2,000 university, hospital, and other research facilities located in all 50 states, the District of Columbia, Puerto Rico, Guam, the Virgin Islands, and points abroad. In recent years, Extramural Research has accounted for more than 80 percent of NIH's total annual budget appropriation.

Work by extramural scientists encompasses virtually all aspects of NIH's research interests. This ranges from basic research that explores the fundamental workings of biological systems, to studies that examine disease and treatments in clinical settings, to prevention and population-based analyses of health status and needs.

Some examples of NIH's partnership with extramural researchers that go beyond the awarding of grants and contracts can be seen below:

Disease Progression in HIV-Infected Women. The National Institute for Child Health and Human Development is funding three research sites to increase understanding of how HIV infection affects adolescent and adult women. The partnership will have research sites at the University of Washington in Seattle, WA; the Gladstone Institute of Virology in San Francisco, CA; and the Rush-Presbyterian-St. Luke's Medical Center in Chicago, IL. Funding will total approximately $3.5 million over five years.

Studies of Racial and Ethnic Disparities in Health. The first trans-NIH collaboration designed to address the DHHS Initiative to Eliminate Racial and Ethnic Disparities in Health is underway. The five-year, $33 million collaboration involves seven NIH institutes, one institute from the Centers for Disease Control and Prevention, eleven universities, and one

medical center. The projects will provide scientists with a better understanding of how social and physical environmental factors interact to impoverish the health of racial and ethnic minorities.

Complex Childhood Cancers. Scientists at the National Human Genome Research Institute and the Lund University in Sweden have developed a method of genetic fingerprinting that can tell the difference between several closely related types of childhood cancer. The method combines innovative technology of gene chips with an artificial neural network (ANN). Using typical diagnostic technologies, the four types of childhood tumors used in the study can be difficult to tell apart and their similar appearance can lead to misdiagnosis and improper treatment.

Expansion of Research in Women's Health. Nine NIH institutes and the Agency for Healthcare Research and Quality have joined with 11 universities in a major new partnership to stimulate women's health research across a variety of disciplines. The program – Building Interdisciplinary Research Careers in Women's Health – seeks to increase the number of researchers working on women's health issues. The nine NIH institutes are the National Institute on Aging, National Institute on Alcohol Abuse and Alcoholism, National Institute of Allergy and Infectious Diseases, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Cancer Institute, National Institute of Child Health and Human Development, National Institute on Drug Abuse, National Institute of Environmental Health Sciences, and the National Institute of Mental Health.

Largest Ever Prostate Cancer Prevention Trial. NIH and a network of international researchers launched the largest ever prostate cancer prevention trial during 2001. The study, which will take 12 years to complete, will involve 32,400 men at 400 research sites across the United States, Canada, and Puerto Rico. The study will determine if two dietary supplements – selenium and vitamin E, can protect against prostate cancer, which is the most common form of cancer in men after skin cancer.

Federal Demonstration Partnership (FDP). The FDP is a cooperative initiative among federal agencies and institutional recipients of federal funds. The FDP was established to increase research productivity by streamlining the administrative process and minimizing the administrative burden on principal investigators while maintaining effective stewardship of federal funds. In its current phase, the FDP boasts sixty-five institutional members, eleven federal agencies, and five professional organizations.

Collaboration with Other Federal Agencies

NIH conducts research in partnerships with other federal agencies, in areas of mutual interest or where the benefits from cooperation are strong. These collaborative endeavors often involve NIH's sister agencies in DHHS, such as the Centers for Disease Control and Prevention (CDC) and the AHRQ and other agencies such as the Department of Energy (DOE) and the National Aeronautics & Space Administration (NASA).

A sampling of NIH's diverse research collaborations in recent years with other federal agencies is as follows:

America's Children: Key National Indicators of Well Being. NIH has a key role in an ongoing collaboration involving 10 cabinet agencies working together to issue a comprehensive annual report on the health and well being of children in the United States. DHHS Secretary Tommy G. Thompson praised the 2001 annual report for showing encouraging trends in childhood poverty, children with at least one working parent, low adolescent birth rates, declining death rate for adolescents, and fewer 10th and 12th grade smokers. The collaboration is a concerted effort by all Federal agencies that compile statistics on children to make this information available to policymakers and the public in a single report.

Diabetes Education for Older Americans. DHHS Secretary Tommy G. Thompson commemorated Older Americans Month in May 2001 by announcing a new campaign to remind older adults with diabetes about the importance of routine blood sugar monitoring, and that Medicare benefits are available to help them do this. The National Diabetes Education Program (NDEP) is a joint Federal collaboration of NIH, the Centers for Disease Control and Prevention, and the Health Care Financing Administration. An estimated 4.5 million Medicare beneficiaries have diabetes.

Drug Discovery, Biological Diversity, and Economic Growth. The Fogarty International Center (FIC) is leading a unique effort that addresses the interdependent issues of drug discovery, biodiversity conservation, and sustainable economic growth. The International Cooperative Biodiversity Groups Program is designed to guide natural products drug discovery in such a way that local communities and other source country organizations can derive direct benefits from their diverse biological resources. Benefit sharing may provide clear incentives for preservation and sustainable use of that biodiversity. Funding for this program is provided by six NIH institutes, the Biological Sciences Directorate of the National Science Foundation (NSF) and the Foreign Agriculture Service of the USDA. The cooperating NIH institutes are FIC, National Cancer Institute, National Institute of Allergy and Infectious Diseases, National Institute of Mental Health, National Institute on Drug Abuse, and the National Heart, Lung, and Blood Institute.

Relationships with Private Industry

NIH works with private industry in a number of ways to further the NIH research mission and facilitate the flow of new biomedical knowledge to the private sector for development and commercialization. Examples of these relationships include education and outreach initiatives, joint collection of health statistics, vaccine research and development, clinical trials, and Cooperative Research and Development Agreements (CRADAs) authorized by the Federal Technology Transfer Act of 1986. In the period from FY 1993-FY 2000, NIH entered into 728 CRADAs with industry covering a wide spectrum of biomedical research with the potential to commercialize new health products for the public.

Breakthrough Cancer Treatment. The National Cancer Institute signed a CRADA with Novartis Oncology to begin follow-up clinical trials of a breakthrough oral drug to treat chronic myelogenous leukemia (CML) using molecular targeting. DHHS Secretary Tommy G. Thompson joined NCI Director Richard Klausner in a news conference announcing FDA fast-track approval of the drug, as well as the CRADA for further research and development. The drug was highly effective in producing high remission rates during short duration clinical trials and marks approval of the first drug that directly turns off the signal of a protein known to cause a cancer. Physicians diagnose approximately 4,500 Americans each year with CML, a disease for which bone marrow transplantation is the only known cure. Clinical trials will also test the possible effectiveness of the drug – called Gleevec – in treating other types of cancer.

Public-Private Partnership Launches Osteoarthritis Initiative. For the first time, a public-private partnership will bring new resources and commitment to research for the progression of osteoarthritis, a degenerative joint disease that is the major cause of disability in people 65 or older. Over a period of 5-7 years, the Osteoarthritis Initiative (OAI) will collect information and define disease standards on 5,000 people at high risk of having osteoarthritis and at high risk of progressing to severe osteoarthritis during the study. The initiative includes public funding from the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Institute on Aging. Private funding comes from GlaxoSmithKline, Merck, Novartis Pharmaceuticals Corporation, and Pfizer. The OAI will spend about $8 million per year.

Heart Disease and Stroke. NIH is one of three agencies of DHHS that have joined forces with the American Heart Association (AHA) to fight heart disease and stroke, America's number one and number three killers. U.S. Surgeon General David Satcher participated in the announcement of the public/private partnership. The Federal Agencies, along with some of their components, signed a Memorandum of Understanding with the AHA to speed progress toward goals set forth in Healthy People 2010, a national health promotion and disease prevention initiative. Two NIH institutes are involved – the National Heart, Lung, and Blood Institute, and the National Institute of Neurological Disorders and Stroke.

Initiative on Prescription Drug Misuse and Abuse. The National Institute on Drug Abuse (NIDA) and several national organizations are participating in a joint public health initiative to raise awareness of recent trends in the misuse and abuse of prescription drugs in the United States. The initiative seeks to inform the public, physicians, pharmacists, and others that prescription drugs can be dangerous, addictive, and even deadly when misused or abused. Joining with NIDA are AARP, the American Academy of Family Physicians, the American Pharmaceutical Association, the National Association of Chain Drug Stores, the National Community Pharmacists Association, the National Council on Patient Information and Education, and the Pharmaceutical Research and Manufacturers of America.

New Test for Lyme Disease. A new test developed with funding from the National Institute of Allergy and Infectious Diseases has been shown to be highly accurate and sensitive for

detecting antibodies to Lyme disease. The new assay, produced by Immunetics, Inc., recently won approval from the Food and Drug Administration for use as a diagnostic test for Lyme disease. The product is the result of years of collaboration in an ongoing effort to improve the ability to diagnose Lyme disease.

New Discoveries about Alzheimer's Disease. Research funded by the National Institute on Aging in a newly developed mouse model shows that a recently identified enzyme, BACE1, is responsible for developing the destructive plaques of Alzheimer's disease. The intensifying focus on BACE1 suggests that a drug could be developed to inactivate BACE1, preventing the buildup of beta amyloid in the human brain.

1.4 Summary FY 2001 Performance Report

In keeping with GPRA requirements, most of NIH's performance goals contain quantitative or otherwise objective targets. Accordingly, in most cases, the basis for performance assessment involves data that are uncontroversial, credible, and open to independent public scrutiny (e.g., material readily available through NIH's website). Where such measures are not available or not useful, GPRA also provides a means for an agency to define performance goals that rely on criteria that are descriptive in nature – through the "Alternative Form" provisions of GPRA (Sec. 1115 (b), P.L. 103-62). This approach is central to the assessment of many of the goals for NIH's research activities.

For any given goal, the strengths and limitations of the data sources used in preparing the annual performance assessment can vary. These issues are summarized in each Part II subsection entitled, "Verification/Validation of Performance Measures and Data Issues." Where there are specific issues about the nature and completeness of a data series for a particular evaluation task, they are identified in the course of this discussion. A comprehensive discussion on NIH's approach to performance assessment can be found in Appendix 1.

Part II provides a goal-by-goal presentation of NIH's performance with respect to all of its goals for FY 2001; significant highlights are presented below. Summary data for NIH's goals for FY 1999, FY 2000, and FY 2001 can be found in Appendix 2.

Research Program

The NIH supports non-Federal researchers working in universities, medical centers, hospitals, and research institutions throughout this country and abroad and also conducts research in its own laboratories. The goal of these research activities is increased understanding of normal and abnormal biological functions and behavior and the development of new, and the improvement of existing, prevention strategies, diagnostics, and treatments diseases and disability. Other important outcomes include the timely dissemination of scientific results and research-based health information and the expeditious transfer of medical research results for further development and commercialization of products of direct benefit for improved health.

Research Outcomes. In October 2001, an NIH GPRA Research Assessment Working Group composed of members of NIH's Advisory Committee to the Director, the Director's Council of Public Representatives, and members of Institute and Center national advisory councils assessed representative sample of 735 Science Advances, Science Capsules, and Stories of Discovery resulting from NIH funded research in fiscal year 2001 (See Appendix 1.) Research Awards and Honors that were bestowed on NIH-funded researchers in fiscal year 2001 and were also reviewed by the Working Group. The independent Assessment Working Group concluded that NIH had substantially exceeded its five qualitative research goals.

Examples of research achievements and progress in FY 2001 include:

- Significant advances resulting from the use of mouse models and DNA microarrays. These tools are used in many ongoing NIH-supported research projects that identified potential new targets for development of pharmacologic drugs to treat human diseases.

- Research into aging has provided new insights pertaining to both biology and demographics. Experiments using animal models identified some basic biologic pathways that may contribute to control of the aging process. In addition, the broad topic of caregiving and disability in an aging population is of considerable importance.

- Striking advances that reveal stem cell plasticity and motility demonstrating the ability of adult stem cell populations to contribute to the structure and function of many tissues. Genetic and molecular studies continue to flourish as information stemming from the Human Genome Project is used to pinpoint genes that contribute to disease.

- Innovation in the development of vaccines. Although considered traditional in approach, vaccines themselves have been modernized. Both recombinant DNA technology and naked DNA are now used to generate new vaccines. Diseases for which vaccines are being produced include otitis media (ear infection), Ebola, dengue virus, AIDS, and Leishmania (parasite). A more effective tuberculosis vaccine is also under development.
- Application of microarray technologies that will provide information as to how genes control cell and tissue function; provide a good vehicle for establishing large DNA databases, are advantageous in identifying specific diseased states, e.g, in analyzing genes that are overexpressed in aggressive gliomas; and provide information on new therapeutic targets for treatment.
- Completing a working draft version of the human genome that covered more than 94 percent of the human genome with over one-third in highly accurate finished form.

- Identifying new HIV/AIDS vaccine concepts (e.g., DNA vaccines, a stabilized HIV envelope protein, novel viral vectors, and HIV regulatory proteins) and advancing those concepts into preclinical testing.

Communication of Results. In addition to its direct support of research studies, NIH continued to proactively communicate scientific results and health information to the medical research community, health care providers, patients, and the public.

Significant FY 2001 achievements and progress in the area of communications include:

- Launching several health education campaigns to reach populations at high risk for certain diseases, including African Americans, Hispanics/Latinos, American Indians, Asian Americans, and Pacific Islanders as well as non-English speaking and low-literacy audiences.

- Strengthening collaborations with other organizations involved in health communications, including public libraries, universities, voluntary health associations, and professional associations of journalists, science writers, and health communicators.

- Developing new web-based tools and other materials to increase the number and diversity of individuals participating in NIH-sponsored clinical trials.

Technology Transfer. An important part of the NIH Research Program is ensuring that medical research results are transferred as quickly as possible to the private sector so they can benefit human health. To enhance technology transfer and protect the public's research investment, NIH patents new drugs and other products developed by its scientists and issues licenses to organizations interested in their commercial application.

Significant FY 2001 achievements and progress in technology transfer include:

- Successfully implementing a web-based training module on technology transfer procedures for NIH intramural researchers and staff.

- Reducing the number of delinquent payments owed to NIH and implementing a new litigation process against infringers of NIH intellectual property rights.

Research Leadership and Administration. To effectively manage NIH's research enterprise, leadership is required with respect to priority setting, grants administration and peer review, and agency management and administrative support.

Significant FY 2001 achievements and progress in research leadership and administration include:

- Continuing to identify emerging public health needs and recommend new program initiatives by convening workshops, conferences, panels, and other meetings designed to exchange information and obtain recommendations from medical and scientific communities and the general public.

- Making rapid progress in improving the organization of NIH's peer review system, enhancing study section operations, and shortening the application-to-award cycle.

- Improving the implementation of the web-based Edison invention reporting system.

- Completing implementation of the recommendations of the Arthur Andersen study to enhance NIH's business operations.

- Exceeding expectations in the expansion of performance-based contracting.

Research Training and Career Development Program

One of NIH's major long-term goals is to promote the development of a highly trained population of scientists who can address the nation's future health-related research needs. To achieve this end, NIH provides extramural training support through various types of grants and programs. A flexible and varied series of high-quality training opportunities is offered, tailored to the needs of recipients who are at different stages of their careers. These training and career development programs are designed to increase the nation's ability to attract and retain the best and brightest minds in biomedical research and to develop a group of well-trained, highly skilled investigators capable of producing the scientific discoveries of the future.

Significant FY 2001 achievements and progress in research training and career development include:

- Maintaining application submission and award rates for the most popular NIH training programs that are comparable to historical rates, demonstrating that NIH's individual fellowships, institutional research training grants, and mentored research scientist and clinical scientist development awards remain popular with the pool of potential applicants and the quality of applications continues to be as high as it has been in the past.

- Continuing the progress made over the last three years in awarding training grants to physicians and other clinicians interested in conducting patient-oriented research, with particular success encouraging young investigators to pursue careers involving clinical research.

- Developing and implementing an improved system for measuring the race/ethnicity of trainees and fellows supported by National Research Service Awards (one of NIH's most important training support programs), a system which allows applicants to designate more than one race and brings NIH into full compliance with OMB guidelines.

Research Facilities Program

NIH's Research Facilities Program has two major responsibilities: a) supporting the construction, renovation, and maintenance of NIH buildings and research facilities located on the intramural (Bethesda) campus and at a number of off-campus field stations; and b) making grants to academic institutions and other non-federal centers of research excellence to support the construction and modernization of research facilities.

Significant FY 2001 achievements and progress with respect to research facilities include:

- Completing construction of the Louis Stokes Laboratories (LSL) on schedule. LSL is a six-story consolidated research facility that replaces existing obsolete laboratory facilities on the Bethesda campus and will be used by a number of NIH Institutes and Centers.

- Continuing progress on the construction of the Mark O. Hatfield Clinical Research Center (CRC), which remains on schedule to be completed in FY 2003. The CRC will become the new heart of NIH's intramural research program, providing a 250-bed research hospital, allied clinical facilities, and adjacent laboratories.

- Proceeding on schedule with the initial phase of construction for the John Edward Porter Neuroscience Research Center (NRC), including the successful demolition of an existing older building (Building 35). The NRC will be a multi-level facility providing a collaborative environment for state-of-the-art neuroscience research on the Bethesda campus, enabling basic scientists and clinical researchers from several Institutes and Centers to work in close proximity.

- Making progress in reviewing and approving in a timely manner the designs submitted by NIH grantees for the construction and renovation of extramural research facilities.

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Part II.
Program Planning and Assessment

This part of the Annual Plan describes NIH's active performance goals and targets for FY 2003, FY 2002 and FY 2001. The presentation is organized according to the three Core Programs that NIH identifies for GPRA purposes: Research, Research Training and Career Development, and Research Facilities. For each program, the Program Description, Context, and Summary of Performance provide an overview of the program along with a *performance goals summary table*, which includes all the goals in that program. Following this overview, the Goal-by-Goal Presentation of Performance Goals and Results provides information regarding the functional areas within each program and *performance goal details*. The details include information about the goal's importance, summary charts that display the performance targets associated with the goal, and summaries of the performance results and data that underlie NIH's assessment of progress toward the goal. To allow the reader to easily identify the status of each target, the following codes are used in the summary charts:

★ **Target Substantially Exceeded** -- Indicates that NIH met certain criteria in addition to those needed to meet the target. An independent Research Assessment Working Group developed the additional criteria on a goal-by-goal basis; they apply only to the qualitative research outcomes goals.

◆ **Target Met or Target Successfully Met** – "Target Met" indicates that NIH's actual performance met or surpassed the stated target for quantitative/objective goals. "Target Successfully Met" applies only to qualitative research outcomes goals. It indicates that NIH met criteria developed by an independent Research Assessment Working Group for that target.

◇ **Target Active** – Indicates when NIH plans to meet the target.

◇→ **Target Not Met and Extended** – Indicates that actual performance fell short of the target and that NIH extended the timeframe for meeting the target.

✖ **Not Met** – Indicates that actual performance fell short of the target and that the target was specific to a particular fiscal year. Therefore, no further action can be taken to achieve the target.

Several appendices at the end of the document provide additional details on NIH activities, the agency's approach to GPRA, and other supporting information.

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2.1 Research Program

2.1.1 Program Description, Context, and Summary of Performance

Program Description and Context. NIH's research activities range widely across the medical research continuum -- including basic and disease-oriented research; observational and population-based research; behavioral research; and clinical research, including research to understand both normal health and disease states, to move laboratory findings into medical applications, to assess new treatments or compare different treatment approaches; and health services research.

While the specific research activities undertaken by the agency's numerous Institutes and Centers -- through the intramural labs or grants to the extramural medical research community -- are many, the universal long-term goals are 1) to increase understanding of normal and abnormal biological functions and 2) to utilize this new knowledge in developing improved prevention, diagnosis, and treatment options for diseases, disabilities, and other adverse human conditions.

Scientific research probes and seeks to understand the unknown. The scientific insights that provide a basis for solutions usually accumulate over many years, and often are derived from the efforts of diverse investigators working on and communicating about differing facets of the problem. Medical discovery is marked by stops and starts, and a vital interplay between theory, experimental evidence, and clinical observations. It is very hard -- if not impossible -- to predict what discoveries will arise or to anticipate the opportunities that such new knowledge will provide. Accordingly, NIH must support research along a broad, and, of necessity, expanding program. NIH's medical research program is a diverse and continually evolving portfolio that reflects the agency's obligation to respond to public health needs, a commitment to support research of the highest scientific caliber, and judgment as to the scientific opportunities that offer the best prospects for new knowledge and better health.

Successful outcomes from the research program mean a continuing flow of high quality research, discoveries of new fundamental knowledge, applications in new therapies, diagnostics, prevention, and new research tools -- from extramural grantees and the intramural laboratories. It also means timely dissemination of scientific results and research-based health information and expeditious transfer of the results of its medical research for further development and commercialization of products of immediate benefit to improved health as an important mandate.

As the strategic principles that broadly guides NIH's research program activities indicate (see below), success in mission achievement also involves effective implementation in several key management/process ("means") areas: notably, leadership in setting research priorities, effective mechanisms for grants management and identifying high quality projects for the portfolio, and effective management/administrative support.

GPRA RESEARCH PROGRAM					
Budget (dollars in thousands)	**FY 1999 Actual**	**FY 2000 Actual**	**FY 2001 Actual**	**FY 2002 Estimate**	**FY 2003 Request**
	$14,580,705	**$16,692,719**	**$19,214,206**	**$21,932,194**	**$25,103,261**

NIH Research Program Activities

Research Outcomes -- NIH's ongoing scientific enterprise. This includes research conducted through grant awards and contracts to individual investigators and organizations in the Extramural Research community. It also includes research conducted at NIH's Intramural labs. The intended long-run outcomes of all these activities are increased understanding of normal and abnormal biological functions and behavior and improved prevention, diagnosis, and treatment of diseases and disabilities.

Communication of Results -- Communicate scientific results and health information to the medical research community, health care providers, patients, and the general public.

Technology Transfer -- Promote the efficient transfer of the new technology forthcoming from NIH research to the private sector to facilitate the development of new drugs and other products of benefit to human health.

Research Leadership and Administration

Priority setting–implementing decision-making mechanisms and policies that ensure NIH research is responsive to emerging health needs, scientific opportunities, and new technologies.

Grants administration and peer review–maintaining effective and efficient grants administration and a high quality of peer review to ensure the most meritorious research projects are considered for funding.

Agency management and administrative support–ensuring that management and administrative functions necessary to support the agency's mission are carried out effectively and efficiently.

Summary of Performance – Research Program

Comprehensive summary tables covering all the goals and targets in NIH's Research Program follow. These tables provide updated information on the status of all of the program's performance targets. More extensive information on each goal, including a chart summarizing the performance results for each target, can be found at the referenced page number.

■ **RESEARCH OUTCOMES**			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
a) Add to the body of knowledge about normal and abnormal biological functions and behavior. **Subgoals[1]:** a.1. Discover innovative approaches for identifying and measuring genetic and environmental factors that contribute to common, complex diseases across populations. a.2. Develop model systems (animal models, cell lines, etc.) that will advance our understanding of disease processes.	**FY 2002 – FY 2003** Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops. ---------- **FY 1999 – FY 2001** Progress in advancing scientific understanding in key fields bearing on our knowledge of biological functions and behavior in their normal and abnormal states.	---------- An independent Research Assessment Working Group reviewed annual progress and made the following assessments: **FY 2001** – Target substantially exceeded. **FY 2000** – Target substantially exceeded. **FY 1999 –** Target substantially exceeded.	Page 64
b) Develop new or improved instruments and technologies for use in research and medicine. **Subgoals[1]:** b.1. Develop new technologies to enable greater understanding of genomic and proteomic information. b.2. Develop biocompatible materials for use in replacing or repairing damaged and non-functioning or missing tissue.	**FY 2002 – FY 2003** Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops. ---------- **FY 1999 – FY 2001** Progress in developing new instrumentation or technologies that enhance capabilities for investigating biological functions and diagnosing and treating diseases and disorders.	---------- An independent Research Assessment Working Group reviewed annual progress and made the following assessments: **FY 2001** – Target substantially exceeded. **FY 2000** – Target substantially exceeded. **FY 1999 –** Target substantially	Page 84

[1] Sub-goals for goals a – d were established for FY 2002 and beyond.

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
		exceeded.	
c) Develop new or improved approaches for preventing or delaying the onset or progression of disease and disability. **Subgoals[1]:** c.1. Identify modifiable risk factors for disease/disability. c.2. Identify, develop, and test new/improved medications for the prevention of disease/disability.	**FY 2002 – FY 2003** Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops. ---------- **FY 1999 – FY 2001** Progress in developing (or facilitating the private sector's development of) new or improved approaches for preventing or delaying the onset of diseases and disabilities – and which reflect NIH responsiveness to emerging health needs, scientific opportunities, and new technologies.	---------- An independent Research Assessment Working Group reviewed annual progress and made the following assessments: **FY 2001** – Target substantially exceeded. **FY 2000** – Target substantially exceeded. **FY 1999 –** Target successfully met.	Page 94
d) Develop new or improved methods for diagnosing disease and disability. **Subgoals[1]:** d.1. Develop and apply powerful new imaging, genetic, and biological technologies to enable early and more precise diagnosis and intervention. d.2. Identify and apply knowledge about factors, including gender, race, ethnicity, and socioeconomic status, to improve diagnostic reliability and treatment response.	**FY 2002 – FY 2003** Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops. ---------- **FY 1999 – FY 2001** Progress in developing (or facilitating the private sector's development of) new or improved diagnostic methods that are more accurate, less invasive, and/or more cost-effective -- and which reflect NIH responsiveness to emerging health needs, scientific opportunities, and new technologies.	---------- An independent Research Assessment Working Group reviewed annual progress and made the following assessments: **FY 2001** – Target substantially exceeded. **FY 2000** – Target substantially exceeded. **FY 1999 –** Target substantially exceeded.	Page 106

[1] Sub-goals for goals a – d were established for FY 2002 and beyond.

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
e) Develop new or improved methods for treating disease and disability[2].	**FY 1999 – FY 2001** Progress in developing (or facilitating the private sector's development of) new or improved treatments that expand therapy options; improve the length and quality of life; and/or are more cost effective -- and which reflect NIH responsiveness to emerging health needs, scientific opportunities, and new technologies.	An independent Research Assessment Working Group reviewed annual progress and made the following assessments: **FY 2001** – Target substantially exceeded. **FY 2000** – Target substantially exceeded. **FY 1999 –** Target substantially exceeded.	Page 115
f) Develop critical genomic resources, including the DNA sequences of the human genome and the genomes of important model organisms and disease-causing microorganisms.	**FY 2003** 1. Finish sequencing of the human genome (accuracy of at least 99.99%). 2. Obtain full-length clones and sequence data for 40,000 mammalian cDNAs. 3. Complete full shotgun coverage of the sequence of the mouse genome; finish 40% of the mouse genome (greater than 99.99% accuracy). 4. Initiate pathogen sequencing projects for additional pathogen genomes (bacterial, fungal and parasitic). 5. Augment the functional analysis of pathogen genome sequences using state-of-the-art technologies, by providing for technology research, development, distribution, and access and supporting functional analysis research. ---------- **FY 2002** 1. Finish two-thirds of the human genome (accuracy of at least 99.99%). NIH grantees will be responsible for half of this target, i.e., one-third of the human genome.		Page 129

[2] This goal will be combined with goal d for FY 2002 and beyond.

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	2. Obtain full-length clones and sequence data for 20,000 mammalian cDNAs. 3. Complete full shotgun coverage of the sequence of the mouse genome; finish 10% of the mouse genome. 4. Complete 3X sequence coverage of the rat genome. 5. Initiate pathogen genome sequencing projects for additional NIH priority areas based upon Blue Ribbon Panel Report. 6. Establish a mechanism to facilitate access to resources, services, and technologies (bioinformatics, scanning, microarrays, genome chips) needed to investigate microbial gene function. 7. Develop technologies that assess, display, and query human genome sequence data to facilitate investigation of how the immune system responds during different disease conditions (i.e., infection, transplantation, autoimmune disease, and other diseases). --- **FY 2001** 1. Worldwide effort completes "full shotgun" of human genome sequence (95% complete, 99.9% accurate). 2. Finish one-third of human genome (accuracy of at least 99.99%). 3. Identify 2,500,000 human single nucleotide polymorphisms (SNPs).	--- 1. The Human Genome Project public consortium succeeded in meeting its target to complete a "full shotgun" of human genome sequence. 2. As of September 30, 2001, 54 percent of the genome was in the completely finished form that has no remaining, closable gaps and an accuracy of 99.99 percent. 3. As of September 30, 2001, the public database that serves as a central repository for SNPs,	

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
		dbSNP, had received submissions for 3,845,467 SNPs for the human genome, 2,421,261 of which are non-redundant.	
	4. Complete 2X depth of coverage toward the working draft of the mouse genome (90% coverage, 99% accurate).	4. 3X depth of coverage of the mouse DNA sequence has been achieved.	
	5. Complete 1X depth of coverage toward the working draft of the rat genome (90% coverage, 99% accurate).	5. The rat sequencing consortium has completed nearly 2X coverage of the rat genome in whole genome sequence reads.	
	6. Complete worldwide sequencing effort of the entire genome of *Plasmodium falciparum*.	6. The sequence of chromosome 2 has been published and preliminary sequence data and annotation are available for chromosomes 10 and 11, (the other chromosome sequences supported by NIH). Worldwide, outstanding progress has been made in sequencing the remaining chromosomes and the complete genome sequence of *P. falciparum* will be published in 2002.	
	7. Complete sequencing of five additional bacterial pathogens and five chromosomes of protozoan parasites.	7. The genome sequences of five bacterial pathogens were published in FY 2001. Also, manuscripts are in preparation for an additional five bacterial pathogens. Sequencing of five chromosomes of protozoan parasites is expected to be completed in FY 2002.	
	8. Augment existing knowledge of pathogen genomes by initiating sequencing projects for at least six additional genomes (bacterial, fungal, parasitic).	8. NIH initiated genome-sequencing projects in FY 2001 for nine pathogens.	
	----------	----------	
	FY 2000 1. Worldwide effort completes "working draft" of human genome sequence (90% complete, 99% accurate). U.S. contributes two-	1. The Human Genome Project public consortium completed a "working draft" of the sequence of the human genome.	

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	thirds of that amount, and NIH contributes 85% of U.S. total. 2. Finish the sequence of at least one human chromosome. 3. Complete sequence of the genome of *Drosophila melanogaster* (excluding heterochromatin). ---------- **FY 1999** 1. Reach U.S. annual production rate of human genomic sequence of 90 million base-pairs. 2. Reach worldwide annual production rate of human genomic sequence of 220 million base-pairs. 3. Total human genomic sequence completed worldwide at the end of FY 1999 at 400 million base-pairs. 4. Complete the sequence of the *C.elegans* genome (97 million base-pairs).	 2. The Human Genome Project public consortium completed the "finished" sequence of two human chromosomes. 3. A consortium of publicly funded scientists, in collaboration with a private company, published the genome sequence of the fruit fly (Drosophila melanogaster) ---------- 1. An annual U.S. production rate of 173 million base-pairs was achieved. 2. An annual worldwide production rate of 265 million base-pairs was achieved. 3. The worldwide completed sequence achieved was 442 million base-pairs. 4. The complete sequence of the *C. elegans* genome was published.	
g) Develop an AIDS vaccine by 2007.	**Annual Targets (FY 2001 to FY 2007)** 1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies. 2. Progress in characterization,	**FY 2001** 1. Advances in the design and development of vaccine strategies during FY 2001 continued to fuel the pipeline of promising HIV/AIDS vaccine candidates. Vaccine candidates and concepts evaluated preclinically in FY 2001 include improved DNA vaccines, a stabilized HIV envelope protein, novel viral vectors, and HIV regulatory proteins. 2. Animal models, especially the	Page 138

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	standardization, and utilization of animal models for evaluating candidate vaccines.	use on non-human primates, continue to provide valuable information in advancing HIV vaccine research and in testing candidate vaccines. Advances in FY 2001 utilized non-human primates in their evaluation of candidate vaccines. In addition, progress was made in development of small animal models (the rat and the mouse) of HIV infection.	
	3. Progress in completion of ongoing trials.	3. In FY 2001, NIH completed seven clinical trials	
	4. Progress in initiation of additional domestic and/or international trials of new or improved concepts and designs, including the progression of promising candidates to larger trials testing vaccine candidates.	4. NIH initiated two new phase II vaccine trials in FY 2001, one domestic and the other in the Caribbean and Brazil. These trials are being conducted under the direction of the HIV Vaccine Trials Network.	
	5. Progress in collaborating with scientists in developing countries and with industry to further promote the development of vaccines for world-wide use.	5. In FY 2001, NIH initiated an international phase II clinical trial through the HIV Vaccine Trials Network. In addition, activities were completed in to increase collaboration with industry which included: a solicitation for additional new HIV Vaccine Design and Development Teams, awarding of five new Vaccine Developmental Resources Contracts to private companies, and signing of a Cooperative Research and Development Agreement with Merck.	
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	FY 2000 1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.	1. Notable progress was made both scientifically and programmatically.	
	2. Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.	2. A variety of animal models were utilized to make important advances.	

■ RESEARCH OUTCOMES			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	3. Progress in completion of ongoing trials. 4. Progress in initiation of additional domestic and/or international trials of new or improved concepts and designs, including the progression of promising candidates to larger trials testing vaccine candidates. 5. Progress in collaborating with industry to enhance opportunities for vaccine development. ---------- **FY 1999** 1. Increases in the research portfolio supporting innovative vaccine discovery. 2. Progress in completion of ongoing trials 3. Progress in initiation of additional domestic and/or international trials of new or improved concepts and designs, including the progression of promising candidates to larger trials testing vaccine candidates. 4. Increased interactions between academic investigators and industry, to enhance opportunities for vaccine discovery and product development.	3. Three ongoing trials were completed. 4. One new trial was initiated. 5. HIV Vaccine Design and Development Team awards made substantially promote university-industry collaboration. ---------- 1. The number and dollar value of awards made for vaccine discovery increased. 2. Of the seven trials started in prior fiscal years, two were completed. 3. Four new trials were begun. 4. Actions were taken to increase the interaction of academic investigators and industry.	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
a) Increase awareness of NIH-sponsored research among health care providers to promote research application.	**FY 2003** Collaborate with the National Committee for Quality Assurance to foster implementation of cholesterol clinical practice guidelines. ---------- **FY 2002** Develop a communications campaign to build support and enhance the recruitment for domestic and international AIDS vaccine trials. ---------- **FY 2001** 1. Use continuing medical education programs based on the web-based Asthma Management Model System to disseminate and encourage the use of clinical practice guidelines on asthma. 2. Complete web accessibility for viewing nursing education programs and establish a once-a-month chat room where program directors will be available to answer questions from nursing students and nurse researchers. 3. Increase awareness of NIDA-sponsored clinical treatment among health care providers. 4. Use a partnership with the American Academy of Family Physicians to increase the knowledge of primary care physicians about the diagnosis and treatment of mental disorders.	---------- 1. As of the end of FY 2001, about 800 physicians had accessed the module on NHLBI's website and completed the course for full Category I credit. Many more physicians had visited the CME site. 2. NINR established a chat room for participants in the NINR Summer Genetics Program to enhance information about the application of genetic advances to nursing. The chat room was averaging 70 messages per month at the end of FY 2001. 3. Seven research-based drug abuse treatment protocols were tested in real-world treatment settings by the network's six pioneering regional research centers in collaboration with more than 35 community treatment programs. 4. NIH engaged in partnership with the AAFP and helped them develop core elements of a training program to include video and online CME programs and case studies; lectures; a quality improvement module for improving care for major depressive disorders; an AAFP monograph "Diagnosis and	Page 147

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
		Management of Depression," mailed to 88,232 AAFP members; a series of mental health patient education handouts on mental health topics; and articles and reports published throughout the year on mental health issues in the AAFP journal.	
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	FY 2000 1. Disseminate and encourage the use of clinical practice guidelines for the treatment of high blood pressure, high blood cholesterol, and other conditions by physicians who provide care to African-American patients.	1. Model cases studies on 11 aspects of treatment for cardiovascular disease were developed. Physicians who treat African-American patients have reached more than 600,000 other health professionals, patients, and members of the public with guidelines-based messages.	
	2. Use telehealth technology and TV cable networks for education projects with nursing organizations and academic institutions: broadcast select conferences and workshops to nursing organizations and academic institutions and add website components that will allow users to interact on-line with live discussions, conferences, and other types of meetings.	2. Enhanced electronic outreach, on-line access to educational conferences, and a National Institute of Nursing Research (NINR) listserve were all created by the end of FY 2001. NINR also collaborated with other organizations to develop a videotape series on End of Life Care.	
	3. Expand the "Not Just Once, But for A Lifetime" mammography campaign to reach health professional organizations, physicians, nurses, and other health and medical practitioners to increase awareness of the importance of mammography screening and the Medicare mammography benefit, and referrals for women, particularly those aged 65 and older.	3. NCI expanded the Breast Cancer and Mammography Education program by the end of FY 2001 by conducting qualitative research to develop and refine health education materials for consumers, emphasizing women 65 years and older, and health professionals. Research conducted with physicians was incorporated into a mammography campaign to reach health professionals.	
	4. Fund a series of demonstration projects applying telemedicine and other technology to improve the speed of reaching heart attack	4. Ten project awards were made.	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	victims with lifesaving treatment. --- **FY 1999** 1. Evaluate the use of clinical practice guidelines on the treatment of high blood pressure and high blood cholesterol by physicians who provide care to African-American patients. 2. Evaluate use of clinical practice guidelines on high blood pressure and obesity.	--- 1. The results of the evaluation are described in FY 2000 Target 1 above. 2. Focus groups to evaluate whether physicians were using the guidelines were completed in FY 2000.	
b) Increase awareness of NIH-sponsored research results among racial/ethnic minorities and high risk, underserved, and/or affected publics.	**FY 2003** 1. Implement a campaign to provide information on noise-induced hearing loss. 2. Use a variety of media approaches (t.v. and radio news inserts, etc.) to communicate the importance of eating 5 fruits and vegetables a day. --- **FY 2002** 1. Develop and disseminate Asian language materials communicating the benefits of mammography. 2. Provide support and technical assistance to NHLBI's Enhanced Dissemination and Utilization Centers to conduct heart-health education projects in high-risk communities. 3. Develop messages and materials to communicate the health implications of obesity. 4. Develop and implement an eye health awareness campaign. --- **FY 2001** 1. Increase awareness of autoimmune diseases (such as rheumatoid arthritis, lupus, and scleroderma) among minority populations who are disproportionately affected.	--- 1. NIAMS's Community Health Center was opened to screen and educate patients from minority populations; distribution of materials in English and Spanish was begun for these populations; and NIH participated in national and local events that reached minority patients and the health	Page 150

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
		professionals who serve them.	
	2. Increase understanding about the seriousness of diabetes and the importance of blood glucose control among African Americans, Asian/Pacific Islanders, and American Indians.	2. Increased awareness was accomplished through five major National Diabetes Education Program awareness campaigns.	
	3. Increase awareness about how to prevent fully preventable noise-induced hearing loss (WISE EARS! campaign) among industrial workers, Hispanic/Latino/Latina individuals, and Native American youth and their parents.	3. Examples of activities for each of the groups included collaborations with the Indian Health Service, Administration for Children and Families, Bureau of Indian Affairs/Department of Interior, and the Department of Education, and participation in conferences, meetings, and exhibits sponsored by the National Hispanic Medical Association and the National Hispanic Heritage Association.	
	4. Increase knowledge among Hispanic parents of the effects of drugs on the brain and encourage them to talk with their children about drug abuse.	4. NIH distributed 140,000 booklets via Hispanic organizations, clinics and Spanish radio public service announcements. NIH also translated a series of fact sheets; four NIDA research reports; and NIDA's popular books on marijuana, preventing drug abuse among children, and treatment principles. Spots for NIDA's public awareness campaign, "Keep your brain healthy. Don't use drugs," were aired on Spanish radio and television stations.	
	5. Increase awareness of the effects of drug abuse among Native American Indians.	5. NIH distributed 150,000 calendars with drug messages to this population via Native American organizations and businesses.	
	6. Develop and implement an AIDS vaccine communication campaign to increase awareness of AIDS vaccines before the initiation of a large efficacy trial.	6. The AIDS vaccine communications campaign will be launched in FY 2002.	
	7. Increase awareness of sports injury	7. NIAMS developed, distributed,	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	prevention among parents.	and promoted a fact sheet about sports injury prevention entitled, *Childhood Sports Injuries and Their Prevention: A Guide for Parents with Ideas for Kids*, to 128 newspapers in 10 states and to more than 2,700 YMCA's and YWCA's.	
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	FY 2000 1. As an activity of the NIH Hispanic Communications Initiative (HCI), conduct a Spanish-language "media summit" that will detail strategies for developing continuous and sustainable working partnerships between NIH information offices, national Spanish-language media outlets, and national Hispanic intermediary organizations.	1. The media summit was held in the first quarter of FY 2001.	
	2. Develop and disseminate easy-to-read and Spanish language health education materials on health issues to targeted special populations.	2. Several NIH Institutes developed and disseminated easy to read and Spanish language materials on various diseases and other health topics.	
	3. Expand programs on anxiety disorders and depression to audiences for whom language or literacy are challenges.	3. A series of five easy to understand booklets on anxiety disorder were developed. Similar materials for depression and bipolar disorder are under development.	
	4. Pursue new outreach and collaboration initiatives to disseminate information and resources on rheumatic diseases in minority populations.	4. An African American Community Partnership was launched.	
	5. Develop and implement diabetes awareness campaigns that target minority populations and their health care providers.	5. Seven diabetes awareness campaigns targeting minority populations and seniors were developed and implemented.	
	6. Develop and disseminate motivational messages related to breast and cervical screening to African American, Hispanic, and Asian communities.	6. Motivational messages on these topics were disseminated to these communities.	
	7. Increase the available information on the benefits of exercise to older people.	7. Information about the benefit of exercise was made available	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	---------- **FY 1999** 1. Establish a centralized site on the NIH home page for access to NIH materials in Spanish. 2. Evaluate several selected NIH outreach programs: cardiovascular health outreach activities for Latinos. 3. Develop and implement NIH information, education, and outreach programs on specific health issues: extend the "Back to Sleep" campaign to minority populations. 4. Develop and implement NIH information, education, and outreach programs on specific health issues: Breast Cancer and Mammography Education Program.	through the news media, health fairs, and professional meetings. ---------- 1. A centralized site was established and launched. 2. An evaluation of the community based outreach initiative "Salud para Su Corazon" was completed. 3. An educational video, outreach to day care facilities, and creation of a coalition of African American organizations to promote back sleeping by infants were completed. 4. NCI continued to implement the Breast Cancer and Mammography Education program.	
c) Increase awareness of NIH-sponsored research results among the general public.	**FY 2003** Launch three new services to enhance the online health information resource, MEDLINEplus. ---------- **FY 2002** 1. Introduce an easily navigable site on the World Wide Web that can increase older adults' awareness of health information and, based on the National Institute on Aging-supported cognitive research findings, enhance the online learning experience for people age 60 and over. 2. Perform a process evaluation of the effectiveness of pap test information materials produced in FY 2001. 3. Develop campaign materials about the importance of calcium from milk and other sources for strong bones. 4. Implement a stroke awareness campaign.		Page 154

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	FY 2001 1. Strengthen relationships with constituency groups nationwide to increase awareness of the latest scientific information about drug abuse and addiction prevention and treatment and to provide a channel for feedback about emerging grassroots issues.	1. NIDA conducted continual outreach with its core constituents around the country. It held biannual meetings and sent out newsletters and other mailings to keep in touch and promote communication between the organizations and NIDA.	
	2. Improve the public's access to health information by expanding the NLM's consumer health information program to ensure that a medical library in every state is working with public libraries and community organizations.	2. By September 30, 2001 there was at least one NLM-supported medical library in every state and Puerto Rico working with public libraries and other community organizations, including faith-based organizations.	
	3. Increase awareness among university presidents, program planners, and policy makers about college drinking and related problems.	3. The target has been extended to include new research findings that will be released in the Report of the Subcommittee on College Drinking, expected March 2002.	
	4. Increase awareness among the general public about the achievements of publicly-funded vision research.	4. The National Eye Institute (NEI) completed a tour of VISION, a traveling exhibit that highlighted the sight-saving results of vision research. The exhibit was displayed in science museums in 26 metropolitan areas with more than 5.3 million people visiting the exhibit through July 2001.	
	5. Increase awareness among young people of the importance of calcium in their diet.	5. NICHD launched the new Milk Matters website for young children and teens on December 1, 2001.	
	6. Increase the number of people who know the symptoms of stroke and rapidly seek treatment.	6. NIH launched "Know Stroke. Know the Signs. Act in Time," a consumer education campaign about recognizing the signs of stroke and acting quickly to get treatment.	
	7. Increase the public's understanding of cancer research, advances, and opportunities.	7. In efforts to increase public understanding of cancer research,	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
		advances and opportunities, the National Cancer Institute initiated a number of activities including distributing almost 2 million publications about breast cancer prevention to women and health professionals; almost 300,000 informational materials for cervical cancer prevention; and 1.1 million 5 A Day related publications to consumers.	
	8. Increase awareness among the general public that drug addiction is a brain disease.	8. NIH developed and distributed materials to its target audiences. The campaign combined public awareness materials, educational materials, speakers, information online, and a wide array of outreach to the general public.	
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	FY 2000 1. Increase the usage of NLM's existing catalog-based databases for books, serials, and audiovisuals by 15 percent.	1. The level of usage increased by 27% over the FY 1999 level.	
	2. Increase the number of "health topics" in the web-based MEDLINEplus to 300.	2. The number of health topics in MEDLINE plus increased to 414.	
	3. Ensure that no less than 85 percent of respondents to a customer feedback instrument rate NLM services at least satisfactory.	3. A survey showed that 98% of users rated NLM services as satisfactory or better.	
	4. Increase collaboration with professional associations of journalists, science writers, and health communicators to increase their coverage of NIH-funded research results.	4. NIH collaborated with these organizations to increase the likelihood that medical research findings will be reported in the media or through health communication programs.	
	5. Implement “WISE EARS!” communications program by developing a coalition of more than 70 groups representing government, industry, the worker, children and older individuals as well as organizations directly committed to preventing noise-induced hearing loss and providing them with resources in order to reach children under 17, adults in mid-life, and older Americans as a	5. NIH developed a coalition of 78 organizations.	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	means to provide information about how to prevent fully preventable noise-induced hearing loss with messages in at least 50% of states by 2001. 6. Expand the outreach of the "Milk Matters" campaign beyond parents and health professionals to focus directly on activities and products that help children and teens recognize the benefit of calcium in building strong bones. 7. Generate a minimum of 30 million media impressions through placements in newspapers and magazines nationwide and on national and local television and radio programs, to raise awareness among all Americans of the importance of eating at least 5 servings of fruit and vegetables a day. ---------- **FY 1999** 1. Implement a system to track customer service interactions, measure response times, and record customer feedback on NLM products and services. 2. Provide a single toll-free telephone number to reach NLM customer service staff. 3. Complete the restructuring of NIMH's mental health education and information dissemination programs. 4. Increase the availability of consumer health information, publications, and reports under NIH's Centralized Consumer Health Information area by 20 percent. 5. Strengthen relationships with universities, voluntary health associations, and other organizations that communicate health and scientific information--to expand the options for communicating NIH research results.	6. New educational materials were developed, strategic alliances formed with professional organizations, and materials distributed to peer and opinion leaders. 7. Mass media activities to raise awareness generated more than 30 million media impressions. ---------- 1. NLM installed software and a program that tracks inquiries, measures response times, and records customer feedback on its services. 2. The toll-free telephone line was established. 3. NIMH developed a new mission statement for the Institute's communications programs. A new Associate Director position was established and filled. 4. The number of on-line publications increased approximately 76%. 5. NIDDK established relationships with 375 public and private organizations to support the National Diabetes Education Program.	

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	6. Develop and implement NIH information, education, and outreach programs on specific health issues: Low Vision.	6. NIH launched the Low Vision program.	
d) Increase awareness of clinical research and support participation in clinical trials.	**FY 2003** Develop messages and materials about participating in clinical studies. ---------- **FY 2002** In partnership with community-based organizations, develop rheumatic disease health education materials and increase awareness of opportunities to participate in clinical studies. ---------- **FY 2001** 1. Develop web-based clinical trials tools that will improve the development, conduct, and ease of participation in NCI-sponsored clinical trials. 2. Improve NCI efforts to increase participation and retain minorities, under-served populations, and the elderly in clinical trials. 3. Educate the public about the importance of NIMH-supported clinical research and interest individuals and their families in participating in clinical studies.	---------- 1. NCI developed a means to dynamically generate a list of trials that can appear on web pages about new drugs and treatments. NCI developed web-based informatics "products" to improve the reporting and exchange of clinical trials information. 2. NIH created the Special Populations Network (SPN), a new $60 million program to address the unequal burden of cancer within certain special population groups. 3. NIMH developed a communications plan to increase awareness of and participation in NIMH intramural and extramural clinical trials. New materials (both web and print) and outreach activities were developed for select trials using target audience research (e.g., focus group testing), literature reviews, and consultation with investigators. NIMH sponsored a workshop and created a handbook to educate investigators on how to recruit locally using the media, the web, advertisements, and community groups	Page 159

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	4. Increase the number of initial contacts about clinical trials with the Patient Recruitment and Public Liaison Office (PRPL). ---------- **FY 2000** 1. Build and maintain networks of communication and support for clinical research between NIMH and consumer and advocacy organizations and professional groups nationally, regionally, and locally. 2. Develop methods and materials to improve communication with minorities and ethnic groups and to encourage them to participate in (NIMH-sponsored) clinical research, thus meeting a critical public health need. 3. Increase visitors to NCI's cancerTrials website and the amount of information about cancer trials to patients, health professionals, the public and the media in all areas including prevention, detection, diagnosis, and treatment. 4. Develop simplified and easy-to-understand informed consent forms to help patients better understand a study's treatments and tests and their possible benefits and risks before deciding whether or not to participate. ---------- **FY 1999** Initiate a broad-based communications and public outreach program to reach physicians, and eventually, community groups and the general public.	4. The Patient Recruitment and Public Liaison Office at NIH received 31,251 contacts in FY 00 and 42,863 in FY 01, an increase of 37%. ---------- 1. NIH initiated the Constituency Outreach and Education Program (COEP). Networks were established with 51 partners in FY 2001. 2. Formative research, including focus group testing, was used to gather information on minority participation in NIMH clinical research in FY 2001. Media activities to increase enrollment included a focus on minority audiences. 3. The total number of users expanded by 33% and the range of information available on the website was considerably enlarged. 4. NCI developed a simplified and easy to understand informed consent form. ---------- A broad-based communications and public outreach program was initiated.	
e) Establish a Clinical Trials Database, as required by the FDA Modernization Act.	**FY 2001** 1. Complete an implementation study to determine the optimal design and function of a toll-free telephone to facilitate access to the Clinical Trials Database.	1. NIH completed an implementation study in March 2001 to determine the optimal design and function of a toll-free telephone service to facilitate access to the clinicaltrials.gov database.	Page 162

■ COMMUNICATION OF RESULTS			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	2. Expand the number of industry-sponsored clinical trials in the database by 250 3. Expand the number of clinical trials in the database sponsored by other federal agencies by 100. 4. Promote the database as a resource for patients, physicians, researchers, community health groups and others. --- **FY 2000** 1. Expand the Clinical Trials Database to include trials from other federal agencies and the private sector. 2. Develop options for implementation of toll-free telephone access to information in the Clinical Trials Database. --- **FY 1999** Develop and implement the Clinical Trials Database.	2. The number of industry sponsored clinical trials was increased by 109. NIH expects to reach 250 in FY 2002. 3. The number sponsored by federal agencies tripled from 104 in FY 2000 to 383 in FY 2001. 4. NIH promoted the ClinicalTrials.gov database as a resource for patients, physicians, researchers, community health groups and others. The site received about 2 million hits per month and hosted approximately 5,300 visitors daily in FY 2001. --- 1. At the end of FY 2000, 800 of the more than 5,000 trials in the database were supported by the private sector or other federal agencies. 2. The final report was completed in 2001. --- Data elements were developed for the database in FY 1999 based on the legislative requirements and discussions with collaborating NIH Institutes and other groups.	

■ TECHNOLOGY TRANSFER			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
a) Increase the number of scientists who have received training in technology transfer.	**FY 2003** 1,000 scientists complete the web-based training module. --- **FY 2002** 200 scientists complete the web-based training module. --- **FY 2001** Seek to have 15% of scientists complete the training module, and/or attend technology transfer seminars. --- **FY 2000** 1. Implement training module. 2. Contact 20% of NIH scientific staff. --- **FY 1999** Contractor development of a web-based training module.	--- Approximately 62% of the scientists attended technology transfer seminars and meetings. --- 1. The training module was activated on the web in the first quarter of FY 2001. 2. By the end of FY 2001, over 60% (2450 of the over 4000 members) of the scientific staff were contacted. --- The training model was completed in FY 2000.	Page 166
b) Develop a system to identify and measure the health outcomes of technologies licensed by NIH.	**FY 2003** Finalize the approach and apply the methodology to 10% of all exclusively licensed technologies that are a part of commercially available products. --- **FY 2002** Develop two case studies to test the proposed methodology. --- **FY 2001** Establish a working group in the Office of Technology Transfer and obtain recommendations on potential outcome measures and sources for obtaining reliable data for those measurements on therapeutic drugs, vaccines and devices.	--- A working group was established to work on the development of health outcomes measures. Recommendations on potential outcome measures will be developed in FY 2002.	Page 168
c) Maintain oversight and protection of the public investment in NIH research	**FY 2002** 1. Implement a data system that includes all license monitoring milestones and benchmarks for all exclusive licenses.		Page 170

■ TECHNOLOGY TRANSFER			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
through increased monitoring of licensee activities.	2. Reduce delinquencies over 180 days and bring that number to zero by the end of FY 2002, except for cases that are being actively negotiated due to the affect on public health. 3. Ensure that all delinquent payments associated with terminated licenses will be submitted to the NIH Debt Collection Officer within 120 days of termination. 4. Perform audits on up to 3 licensees during the year, if warranted. --- **FY 2001** 1. Recruit and select personnel to establish a special license-monitoring unit to provide oversight of licensee progress in developing and commercializing technologies licensed from NIH. 2. When indicators show that sales and royalty information may be incorrect, conduct audits of up to 3 licensees during the year. 3. Reduce the number of delinquent payments over 180 days by 50% from the number in place at the end of FY 2000. 4. Reduce the number of terminated licensees with outstanding royalty amounts owed by 10% from the number at the end of FY 2000. 5. Develop and implement a process to refer infringers of NIH intellectual property rights to the Department of Justice with recommendations for bringing a federal law suit against such entities.	--- 1. A recruitment effort was executed, but qualified candidates were not found. The recruitment for these positions will be re-announced in FY 2002. 2. An outside group, hired by NIH, audited five licenses. 3. The number of delinquent payments over 180 days was reduced by 55% from the number in place at the end of FY 2000. 4. NIH exceeded its target by reducing the number of terminated licenses with outstanding balances by 43%. 5. A process for referring infringers of NIH intellectual property rights to the Department of Justice was developed and implemented. One of three cases initiated in FY 2001 was settled.	

■ **PRIORITY SETTING**			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
a) Ensure that NIH-supported research reflects the changing nature of scientific opportunities and public health needs. Note: This goal is part of the normal research grant selection process and will not be continued past FY 2001.	**Annual Target** Sponsor Institute and Center workshops and panels that assess scientific progress and opportunities and identify emerging public health needs. Incorporate findings and recommendations from these workshops and panels into updated proposal submission requests for Institute and Center research programs.	**FY 2001** NIH's Institutes and Centers convened many workshops and other meetings that resulted in new programmatic initiatives being issued in FY 2001. ---------- **FY 2000** Numerous workshops and other meetings were convened that resulted in new programmatic initiatives in FY 2000. ---------- **FY 1999** Numerous workshops and other meetings were convened that resulted in new programmatic initiatives in FY 1999.	Page 176

■ GRANTS ADMINISTRATION AND PEER REVIEW			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
a) Improve electronic Research Administration (eRA) technology by developing capability for end-to-end electronic research administration by 2004.	**FY 2003** Pilot-test electronic receipt of simple (non-clinical, non-human) competing R01 applications. --- **FY 2002** 1. Release NIH Commons modules in the new architecture. 2. Scan all incoming competing R01 applications in preparation for pilot testing receipt of R01 applications in 2003. --- **FY 2000** 1. Full deployment of key eRA business process modules. 2. Implement electronic progress reporting with all 65 newly on-line institutions participating in the Federal Demonstration Partnership. 3. Begin pilot testing of progress reporting for multi-project mechanisms. --- **FY 1999** 1. Design and test new systems. 2. Streamline post-award reporting while continuing to ensure appropriate oversight and enhancement of recipients' compliance with reporting and accountability requirements.	--- 1. Key business process models in NIH Commons were made widely available. 2. The 65 research universities and non-profit centers participating in the FDP pilot-tested the new NIH Commons modules. NIH expects to complete implementation in FY 2002. 3. All business process reengineering for progress reporting has been completed. The technological infrastructure necessary for development of the system in the J2EE environment has been put in place. Pilot deployment is scheduled for FY 2002. --- **FY 1999** 1. The Electronic Notice of Grant Award (NGA) system was pilot tested in FY 1998 and fully deployed in FY 1999. 2. E-SNAP began receiving the first electronic applications in a limited pilot.	Page 180

■ GRANTS ADMINISTRATION AND PEER REVIEW			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
b) Ensure proper stewardship of public funding for research.	**FY 2003** Provide Internet-accessible resource information and/or tools for implementing institutional compliance programs. --- **FY 2002** Publish a compendium of observations and examples of compliance in action in the conduct and administration of sponsored programs at NIH's recipient institutions. --- **FY 2001** 1. Create an organizational component within NIH with FTEs devoted expressly to compliance-related activities. 2. Perform a minimum of 10 compliance site visits.	--- 1. In the last quarter of FY 2001 the Division of Grants Compliance and Oversight was established within the Office of Policy for Extramural Research Administration, Office of Extramural Research, NIH. 2. Eight proactive compliance site visits were completed.	Page 183
c) Ensure that the NIH peer review process keeps pace with current advances in research and that the expertise of peer reviewers is appropriate for the needs of modern science.	**FY 2003** 1. Implement modifications to 4 Integrated Review Groups (IRGs) based on recommendations of the Panel on Scientific Boundaries for Review (PSBR), the Steering Committees, and Study Section Boundaries (SSB) Teams. 2. Complete formation of all Steering Committees and SSB Teams. --- **FY 2002** 1. Increase number of Steering Committees and SSB Teams to 10. 2. Complete the formation of all external IRG Advisory Groups. --- **FY 2001** 1. Create 4 Steering Committees and their respective SSB teams. 2. Increase the number of external IRG Advisory Groups to 14. **FY 2000**	--- 1. A total of 7 Steering Committees and their respective SSB teams were created. 2. A total of 19 external IRG advisory groups were created.	Page 185

■ GRANTS ADMINISTRATION AND PEER REVIEW			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	1. Complete Phase 1 of the PSBR and develop an implementation plan for Phase 2. 2. Double the number of external IRG Advisory Groups from 3 to 6. ---------- **FY 1999** Conduct various assessments of the functions and organization of NIH study sections.	1. Phase 1 final report was completed and Phase 2 implementation was initiated. 2. Ten external advisory groups were formed. ---------- The assessments were completed.	
d) Develop innovative business practices to facilitate government/public interactions.	**FY 2003** Evaluate the results of the simplified Streamlined Noncompeting Award Process (SNAP) pilots and make recommendations. ---------- **FY 2002** Pilot-test ways to further simplify NIH's SNAP. ---------- **FY 2001** Further facilitate expediting the processing of the most meritorious grant applications by reducing the receipt-to-award cycle from 9-10 months to 6-7 months. ---------- **FY 2000** Expedite the processing of the most meritorious grant applications by extending to all NIH Institutes the use of expedited en bloc Council review procedures. ---------- **FY 1999** Identify approaches to expedite the processing and award of grant applications.	---------- En bloc Council concurrence was introduced in 13 Institutes. These Institutes made awards to the most meritorious Type 1 grant applications in approximately 6-8 months from application receipt. ---------- A policy announcement encouraging adoption of, and providing guidance for, expedited procedures was prepared and disseminated. ---------- A procedure called en bloc concurrence was established to significantly expedite the awards process.	Page 188
e) Improve grantee reporting of inventions developed with federal funds.	**FY 2003** Deploy a redesigned Edison system to 350 grantee/contractor organizations. **FY 2002** Integrate Edison into the Federal		Page 191

■ GRANTS ADMINISTRATION AND PEER REVIEW			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	Commons (a governmental electronic grants and contracts administration system). --- **FY 2001** 1. Identify ways to improve the quality of historical invention reporting data. 2. Further educate constituents of their invention reporting obligations. --- **FY 2000** Fully establish the Edison system for use by all grantee institutions, and expand its use to other government agencies. --- **FY 1999** Enhance recipient compliance with reporting and accountability requirements.	--- 1. Additional full-time staff were added to allow for a more thorough analysis of historical records. 2. NIH officials responsible for invention reporting participated in all proactive compliance site visits in FY 2001, and made formal presentations at numerous national meetings of academic technology transfer and grants administration professionals. --- The Edison system was fully established and is capable of being used by all grantee institutions. --- 189 grantee institutions were using Edison (40% increase over 1998 level). Memoranda of Understanding with several federal agencies were in use.	

■ AGENCY MANAGEMENT AND ADMINISTRATIVE SUPPORT			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
a) Implement the recommendations of the Arthur Andersen, Inc. study of administrative practices and costs at NIH.	**FY 2000** Complete the implementation of all recommendations as decided upon by the NIH Director and the IC Directors. --- **FY 1999** 1. Complete NIH Director and IC Directors review and decision-making for all recommendations. 2. Implement recommendations related to the Chief Information Officer and the Chief Financial Officer.	NIH completed implementation of the 76 approved recommendations during FY 2001. --- 1. Arthur Andersen made 80 recommendations for NIH implementation in its final report. The NIH Arthur Andersen Implementation Oversight Committee chose not to accept 4 recommendations, leaving 76. 2. CFO and CIO recommendations were implemented.	Page 196
b) Improve the efficiency of the small acquisition process by continuing to expand the Purchase Card Program.	**FY 2003** 1. $230 million in orders. 2. 395,000 orders/transactions. --- **FY 2002** 1. $210 million in orders. 2. 365,000 orders/transactions. --- **FY 2001** $200 million in orders. --- **FY 2000** 1. $160 million in orders. 2. 3,600 people trained to use cards. 3. 2,000 card holders. --- **FY 1999** 1. $110 million in orders.	--- Dollar volume of purchase card orders was $196 in FY 2001. --- 1. $173 million in orders were made. 2. The total number of persons trained increased to 3,922 by the end of FY 2001. 3. Total number of purchase cardholders reached 1,729 in FY 2000 and 1,866 cardholders at the end of FY 2001. --- 1. $130 million in orders were made.	Page 198

■ AGENCY MANAGEMENT AND ADMINISTRATIVE SUPPORT			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	2. 3,000 people trained to use cards. 3. 1,600 card holders.	2. The total number of persons trained increased to 2,860 and reached 3,391 in FY 2000. 3. The total number of cardholders increased to 1,485 and reached 1,729 by FY 2000.	
c) Expand the use of Performance Based Contracting (PBC).	**FY 2003** Allocate $226.0 million of the available NIH contracting dollars to PBC-eligible contracts. --- **FY 2002** Allocate $207.0 million of the available NIH contracting dollars to PBC-eligible contracts. --- **FY 2001** Allocate $21.2 million of the available NIH contracting dollars to PBC-eligible contracts. --- **FY 2000** Allocate $19.8 million of the available NIH contracting dollars to PBC-eligible contracts.	--- The dollars allocated to PBC contracts totaled $36.5 million. --- The dollars allocated to PBC contracts totaled $198.5 million.	Page 201
d) Identify and pilot new approaches to providing human resource services which increase manager satisfaction with personnel system flexibility and ease of use.	**FY 2001** Complete distribution of the final year management satisfaction survey, interviews, and collect and analyze data for the final report due in 2002. --- **FY 2000** A 10% increase in manager satisfaction with personnel system flexibility and ease of use as reflected in the 1999 survey outcome against the 1997 baseline. --- **FY 1999** Complete the delegations of authority and related training.	Data has been collected and is being analyzed. A report is being drafted for release in 2002. --- Data has been collected and is being analyzed to determine what the final impact of increases in personnel system flexibility has been on manager satisfaction with human resources servicing. A final determination on the degree of satisfaction will be available in FY 2002. --- Delegations completed and related training provided to managers.	Page 203

■ AGENCY MANAGEMENT AND ADMINISTRATIVE SUPPORT			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
e) Recruit and retain highly qualified extramural investigators to biomedical/ behavioral research through the use of student loan repayment programs.	**FY 2003** 1. 50% of HDR awardees are from health disparities populations. 2. 75% of eligible sites use the CIR for recruitment. 3. 75% of applicants apply because of the opportunity to participate in the CIR. 4. 25% of CR awardees are first time grant or other award recipients. 5. 50% of ECR applicants are in training or have recently commenced their research careers. 6. 50% of HDR applicants are in training or recently commenced their research careers. 7. 25% of PR awardees are first time grant or other award recipients. 8. 75% of past participants conduct contraception and/or infertility research two years after completing the CIR. 9. 50% of ECR awardees attend educational and/or technical assistance workshops, seminars and other educational mechanisms and are encouraged to apply for small grant support in their 2nd or 3rd year of the program. 10. 50% of HDR awardees attend educational and/or technical assistance workshops, seminars and other educational mechanisms and are encouraged to apply for small grant support in their 2nd or 3rd year of the program. --- **FY 2002** 1. 50% of eligible sites use the CIR for recruitment. 2. 50% of applicants apply because of the opportunity to participate in the CIR.	These targets will be reported on in February 2004 and February 2003 as appropriate.	Page 205

■ AGENCY MANAGEMENT AND ADMINISTRATIVE SUPPORT			
Performance Goal	**FY Targets**	**Actual Performance**	**Details**
	3. 15% of CR awardees are first time grant or other award recipients. 4. 30% of ECR applicants are in training or have recently commenced their research careers. 5. 30% of HDR applicants are in training or recently commenced their research careers. 6. 15% of PR awardees are first time grant or other award recipients. 7. 50% of HDR awardees are from health disparities populations. 8. 50% of past participants conduct contraception and/or infertility research two years after completing the CIR.		
f) Implement government-wide initiative on delayering management levels and streamlining organization.	**FY 2003** Complete delayering for each organizational unit identified. --- **FY 2002** 1. Complete assessment of NIH organizational level structure and rationale for current patterns. 2. Identify organizational units for delayering. 3. Develop implementation plans to accomplish delayering for each organizational unit. 4. Develop specific numeric targets for the implementation plans.	These targets will be reported on in February 2004 and February 2003 as appropriate.	Page 209

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2.1.2 Goal-by-Goal Presentation of Performance Goals and Results

2.1.2.1 Research Outcomes

NIH's research Institutes and Centers (ICs) maintain extensive medical research programs on numerous topics in their areas of focus. In addition to providing grant support to the extramural research community through a competitive proposals process, most of the ICs also conduct their own research in NIH's intramural laboratories. Each year, NIH receives some 40,000 proposals to initiate new research from the most promising and productive scientists at universities and research centers throughout the country -- and, where special opportunities exist, from scientists abroad.

NIH identifies goals and a budget strategy annually to maximize support for basic biomedical research, to promote health, and to better understand the biological and behavioral basis for disease to improve prevention and treatment of human disorders.

The nation's investment in medical research has a long history of success. In recent years, NIH has been able to report annually on advances that represent outstanding achievements in science. Typically, these achievements are the result of past investments made with the belief that medical research will lead to improvements in the nation's health. The federal effort devoted to medical research, combined with private sector efforts, can and does, improve the length and quality of our lives.

As indicated earlier (see Part I), NIH's numerous research activities are aggregated for GPRA planning and assessment purposes. This is done due to the cross-cutting nature of disease and scientific discovery. By aggregating activities that are intrinsically collaborative and complementary, the significance of any particular activity that contributes in a major way to the whole is neither omitted nor minimized. Although each of the ICs has a specific research orientation, there are many commonalties. Most obvious are the shared technical approaches to medical research. Also important, but perhaps less well understood, is the fact that multiple ICs often address different aspects of the major health problems faced by our citizens. Disease is typically systemic, influenced by multiple factors and affects more than one organ or body system. Diverse expertise is usually required to fully understand a disease's etiology, diagnosis, treatment and prevention -- and the efforts of many ICs need to be brought to bear on a particular disease or disability. Reporting on NIH research outcomes by ICs rather than by research topics would yield overlapping and confusing information.

Scientific research is best viewed as an enterprise for the long run – to account for the intrinsic difficulties and uncertainties of probing the unknown. Discoveries and significant advances typically emerge in an uneven way over time and are, as a practical matter, largely impossible to predict in advance. Once in hand, however, progress can often proceed rapidly. Accordingly, NIH's performance goals for the Research Program focus on broad, long-run achievement in key areas that reflect the agency's mission.

Performance Goal Details – Research Outcomes

Goal a) Add to the body of knowledge about normal and abnormal biological functions and behavior.

Clinical advances occur in the context of a body of knowledge developed by basic and applied biomedical researchers. A great deal of this body of scientific knowledge is accumulated in stepwise fashion. Investigators strive to understand broad processes of health and disease (for example, how genes are expressed or what causes cancer metastasis) by elucidating the molecular factors, chemical reactions, and biological mechanisms that contribute to the processes.

Progress in treating the complex diseases that affect our society, which include heart disease, diabetes, cancer, AIDS, hepatitis, mental illness, and many others, is abetted by an understanding of genetic and environmental mechanisms that are involved. Advances that seem to happen overnight, such as the emergence of a useful pharmacological drug or an understanding of a disease etiology, are usually based on a body of knowledge that was accumulated over many years. When a host of investigators use complementary approaches to address related questions, incremental advances can be translated into improved public health.

Both basic and clinical research constitute the science assessed under Goal a. The research considered within this goal is intended to expand the body of basic scientific knowledge, to increase understanding of health and disease, and to provide concrete information that can be applied to improving health and health care.

For fiscal years 1999-2001, NIH measured its success under this goal against the broad target of progress in advancing scientific understanding. For fiscal years 2002 and 2003, NIH has established two representative subgoals to better define NIH's research plans under this goal. These subgoals focus on genetic and environmental factors that contribute to common, complex diseases across populations, and on development of model systems to advance our understanding of disease processes. The importance of these subgoals is detailed below.

Subgoal a.1. Discover innovative approaches for identifying and measuring genetic and environmental factors that contribute to common, complex diseases across populations.

Mankind is plagued by diseases of various origins and manifestations. Congenital and acquired diseases alike affect all populations, but between regions, ages, genders, and races, the same disease may range from mild to severe and from simple to complex. Sorting out the reasons for the variable expression of symptoms, virulence of pathogens, and toxicity of compounds is a major challenge facing scientists worldwide. The issue of nature *versus* nurture, or genetics *versus* environment, is at the heart of many investigations into the factors responsible for these variables, and it is only recently that technology has empowered researchers to distinguish the influences imposed by the genetic makeup of an individual from the contributions of chemicals

and antigens in each individual's surrounding environment. Recent advances in toxicology and signal transduction biology have aided greatly in eliminating many black boxes from our concepts of biology and have provided a link between the extracellular stimuli of the environment and genetic elements in the nucleus using complex biochemical pathways.

NIH-supported investigators are asked to bring to bear all available biotechnology and innovation upon data arising from the genome project, proteomics, and myriad bioinformatics platforms so that an integrated approach can be taken to understanding the complex interactions between genetics and the environment and their influences on the outcome of disease. Remarkable progress has been made in the discovery of new high throughput screening (HTS) technologies providing volumes of biomedically relevant data. Disparate and asynchronous forms of wet lab data are generated from flow cytometry, mass spectrometry, immunoassays, and microarrays, and these data must be interfaced and meshed with clinical data in order to apply what is known towards individualized medicine. Armed with databases of demographics from clinical trials and epidemiologic studies, population-based metabolic profiles, and single nucleotide polymorphisms (SNPs), investigators are charged with developing innovative approaches to the analysis, identification, and measurement of the unique contributions of the genome and environmental factors to disease across the diverse makeup of the human race.

Subgoal a.2. Develop model systems (animal models, cell lines, etc.) that will advance our understanding of disease processes.

The elucidation of drug mechanisms and disease processes was greatly facilitated when the guinea pig was developed as a prototypical model system for biomedical research. That progress has been accelerated time after time following reports of diseases being modeled in other rodents, including mice, rats, and rabbits, as well as completely different phylogenetic categories including birds, amphibians, and fish. Moreover, innovative and perceptive scientists have discovered that some studies are more efficiently conducted in yeast, worms, and flies — species that have now become ubiquitous model systems for both academia and industry. Even the common chicken egg has become an inexpensive but essential model system for studying the complexities of development and angiogenesis. Conversely, other diseases are best modeled in non-human primates, even if these experiments come at great expense and fuel public controversy.

In vitro systems have also become paradigms for mechanism studies. Much of what is known today about cancer initiation and suppression, angiogenesis, cholesterol utilization, the interplay of cytokines or hormones and their receptors, and the physical interactions between cellular constituents within various tissues comes from in vitro model systems. Many questions in the basic biology and biochemistry of disease processes remain unanswered, however, and are partly due to a lack of models suitable for multi-gene or multi-protein defects or deficiencies.

Investigators advance our current understanding of normal and abnormal biological functions by unraveling the complex layers of interactions of proteins within networks, feedback mechanisms, and signaling cascades. Knockout and transgenic animals must continue to be created as novel *in vivo* model systems. In light of the complexities inherent in some disease processes, the need for more intricately designed models will include animals in which the expression of genes can

be regulated and others that have two or more genes eliminated from their genome. Regardless of the type of model system being developed – *in vivo*, *in vitro*, cell-free, or even *in silico* – the challenges facing researchers today will demand creativity, innovation, and boldness to develop new models and new kinds of models in order to continue accelerating the elucidation of disease mechanisms that has been seen in recent years.

Annual Performance	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Progress in advancing scientific understanding in key fields bearing on our knowledge of biological functions and behavior in their normal and abnormal states.	★	★	★		
a.1. Discover innovative approaches for identifying and measuring genetic and environmental factors that contribute to common, complex diseases across populations:					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇
a.2. Develop model systems (animal models, cell lines, etc.) that will advance our understanding of disease processes:					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇

★ Target Substantially Exceeded	◆ Target Successfully Met	◇ Target Active	✖ Target Not Met

Summary of Performance Results

- **The Assessment Working Group was unanimous in their conclusion that NIH substantially exceeded the goal of adding to the body of knowledge about normal and abnormal biological functions and behavior**. The Working Group unanimously agreed that remarkable advances were made in research areas across the NIH portfolio. In their discussion of research outcomes, a number of themes emerged. The Working Group discussed striking advances that reveal stem cell plasticity and motility and agreed that NIH has pioneered research demonstrating the ability of adult stem cell populations to contribute to the structure and function of many tissues. Genetic and molecular studies continue to flourish as information stemming from the Human Genome Project is used to pinpoint genes that contribute to disease.

  In addition, significant advances have resulted from the use of mouse models and DNA microarrays. The Working Group noted that those tools were used in many ongoing NIH-supported research projects that identified potential new targets for development of pharmacologic drugs to treat human diseases. In addition, significant advances were made in basic science, particularly structural biology. The NIH portfolio includes impressive studies relating to aging, as well as noteworthy research that focuses on neuroscience and behavior.

The NIH's institutes and centers submitted 310 science advances, science capsules, and stories of discovery (tabulated at the end of this section) under goal a for FY 2001. In the judgment of the assessment working group, the NIH has "substantially" exceeded its target in adding to the body of knowledge about normal and abnormal biological processes and behavior (see *Performance Assessment Approach* criteria above for "substantially exceeding" goal).

In FY 2000, the Assessment Working Group unanimously concluded that NIH had substantially exceeded the goal of adding to the body of knowledge about normal and abnormal biological functions and behavior. The research evaluated by the group resulted in significant new understandings of biological and behavioral processes, yielded answers to long-standing, important biological and behavioral questions, and had the potential for translation into new or improved technologies, diagnostics, treatments, and preventive strategies. The Working Group also emphasized the wealth of developments related to the discovery of genomic information about humans, model organisms, and disease-causing agents, as well as the ongoing impact of the explosion in genomic information and genetic technologies, and its vast potential in the future. Advances in genetics affected every substantive area discussed by the Group, including cancer, developmental biology, infectious diseases, neuroscience, cardiopulmonary biology, endocrinology, clinical and population studies, and health care delivery.

In FY 1999, the Assessment Working Group concluded the outcomes demonstrated that NIH had sustained the excellence and responsiveness of the research system–an important achievement–while demonstrating willingness to take research risks necessary to advancing biomedical knowledge, and ultimately human health. In their discussion, members of the Working Group identified a number of important themes or categories of research outcomes, discussed the significance of these types of findings, and highlighted a number of research outcomes that they judged to be especially noteworthy.

Research Outcomes and Their Significance

The Working Group agreed that there have been numerous and wide-ranging advances. These advances, which are a source of new knowledge about basic biological processes, are highly relevant to disease biology and treatment.

Among the many areas where NIH-supported research exceeded the goals, research into adult stem cells is one of the most exciting. Investigators are learning that stem cells derived from adult tissues have far greater ability to assume specialized function than was previously known. Stem cell researchers appear to be at the threshold of an entirely new field that carries vast therapeutic potential.

There continues to be important developments in genetics and genomics–fueled by tools that come out of the Human Genome Project. Substantial advances were made in understanding the biology of diseases that affect nearly every organ system, including heart disease, cholesterol absorption in the intestine, autism, Parkinson's disease, Fanconi anemia (the hematological system), and interstitial lung disease. Progress was made toward increasing the understanding of

some rare diseases and also in the understanding of complex conditions where a variety of genes contribute to disease. Examples of complex diseases where advances occurred are Crohn's disease and type 2 diabetes.

As multiple genes for complex diseases are identified, the information can be used to make animal models that come ever closer to approximating the human disease condition. Animal models are used to study basic biology and as tools for investigating potential new treatments. Two very different conditions, deafness and type 2 diabetes, exemplify areas where animal models have been useful.

Another valuable tool that is relatively new is DNA microarray technology (DNA "chip"). The DNA chip is a piece of glass the size and shape of a microscope slide that contains drops of DNA arranged in a grid. Using the DNA chip in a well-designed experiment, an investigator can monitor the expression of every gene in the genome. The DNA chip has provided information about gene expression patterns under various conditions. Improvements in cancer diagnosis may turn out to be a practical benefit of DNA microarray technology.

Many NIH-supported studies have reached the exciting point where potential targets for new therapies have been identified, opening the door for practical approaches to disease treatment and prevention. Areas where potential new targets for development of pharmacological drugs have been identified include Alzheimer's disease, ischemic brain and heart, some post-surgical difficulties, hepatitis C, conditions relating to cholesterol transport, osteoporosis, osteoarthritis, malaria, and sleeping sickness.

A basic science advance that stands out as a landmark accomplishment is the determination of the crystal structure of a key enzyme in life processes, *RNA polymerase II.* This enzyme is part of the gene expression apparatus of the cells of all plants and animal, and knowledge of its structure has important implications for all of biology.

Research into aging has provided new insights pertaining to both biology and demographics. Experiments using animal models identified some basic biologic pathways that may contribute to control of the aging process. In addition, the broad topic of caregiving and disability in an aging population is of considerable importance.

In the area of behavior and neuroscience, advances continue to be made regarding brain chemistry, pleasure-seeking behavior, drug addiction, and relapse.

Stem Cells

Stem cells are relatively undifferentiated cells that have the ability to divide and differentiate (take on the specialized function of an organ or tissue). Previously, it was believed that stem cells derived from adults could only differentiate into a limited range of tissues. However, recent studies in experimental animals showed that when adult stem cells were taken from a donor animal and transplanted (injected) into a recipient, the transplanted cells were able to differentiate into a broader range of tissues. In other words, adult stem cells appear to have greater "plasticity" than was previously believed. Another important observation is that the

injected cells appear to migrate to the site where they are needed. Therefore, adult stem cells appear to have "motility".

Bone marrow is a source of hematopoietic stem cells. It was known that hematopoietic stem cells could differentiate into mature blood cell types, including red and white blood cells. Recently, investigators studying a mouse model of a fatal liver disease (hereditary tyrosinemia type I) showed that purified hematopoietic stem cells could restore normal liver function in animals with the disease.

Other studies showed that transplanted adult hematopoietic stem cells could be used to regenerate heart muscle tissue and vascular tissue after an experimentally-induced heart attack. In that study the injured tissue seemed actually to attract the injected cells. In a different study, scientists found that stem cells derived from the pancreas of an adult mouse could be used to restore liver function in another mouse. Another striking finding was that adult bone marrow cells injected into the mouse circulatory system could find their way to a damaged brain and differentiate into neuronal cells.

A very dramatic demonstration of the plasticity and motility of adult hematopoietic stem cells was performed using a single donor cell. The study used female mice whose bone marrow cells were completely destroyed by irradiation. Normally, an animal whose bone marrow cells are completely destroyed by irradiation would not survive. However, some of these irradiated female mice were given a single purified hematopoietic stem cell from a male donor mouse. After a year, five of the female mice had survived. When the tissues of the surviving animals were examined, scientists found cells with male Y chromosomes in the liver, lungs, gastrointestinal tract, and skin.

The presence of the Y chromosome in these tissues indicates the presence of cells derived from the single, injected male donor cell. This study has important implications. It shows that adult hematopoietic stem cells may have tremendous therapeutic potential (if they behave in humans as they do in mice). For example, stem cells derived from a patient's own bone marrow might someday be used to repair a damaged organ. The cells could be used directly to repair and replace the damaged organ; alternatively, since the cells appear able to migrate to the site where they are needed, a therapy may be developed that uses migrating cells to deliver pharmacological agents directly to sites needing repair. Migrating cells might also be used as a mechanism to deliver gene therapy to the site where needed.

The brain also contains stem cells. In adults, the generation of new neurons occurs in regions of the brain that contain neural stem cells. This normal process is termed "neurogenesis." Some of the factors that stimulate neurogenesis are exercise, brain injury, dietary modifications, and mental activity (learning). Stress and aging seem to impair neurogenesis.

The specific type of brain cell that the neural stem cell develops into depends on the brain environment of the stem cell, including the presence of specific growth factors. If scientists could learn more about the brain factors that are necessary to stimulate neurogenesis, they might be able to enhance cell repair in the aged, injured, or diseased brain.

In a recent study, neural stem cells were isolated from adult rat spinal cord and grown in culture with the growth factor FGF-2. The cultured cells formed both neurons and glial cells (another type of cell found in nervous tissue). When cultured cells were transplanted back into the brain of another adult rat, the transplanted cells differentiated into different cell types depending on the brain region to which they were transplanted. The investigators surmised that different environmental cues were present in the different brain regions.

In another study, investigators looked at the effect of the brain factor cystatin C on development of neural stem cells. They found that both cystatin C and FGF-2 stimulated the survival and growth of neural stem cells in culture. It is not yet known if cystatin C levels decline in aging, and if so, whether a decline in this factor contributes to the low level of neurogenesis seen in aging.

Genes and Genetic Diseases

The Working Group noted that the body of knowledge about the genetic basis of human disease is increasing at an accelerating pace and that researchers are applying that knowledge to the practical objective of finding treatment and cures for genetic diseases. They agreed that NIH and the Human Genome Project have set a new standard for disseminating information, and that the NIH's approach to sharing data openly has raised the bar for thinking about what is meant by "dissemination" and what is meant by "timeliness." The fact that NIH has insisted on making all of the data available on the web, essentially as soon as it is produced, has had tremendous positive impact on the entire field.

Advances in the area of hereditary blindness have been remarkable. Leber's Congenital Amaurosis (LCA) is one of several forms of blindness collectively known as retinitis pigmentosa. LCA accounts for approximately 11 percent of patients with early onset retinal degeneration; currently, there is no treatment for LCA or related early onset retinal degenerative diseases. However, right now there is tremendous hope for a cure, since the disease was recently cured in a dog model.

One of the genes that can cause LCA when mutated is *RPE65*. Dogs used in the study (blind Swedish Briards) have a mutation in the *RPE65* gene that is identical to a mutation that causes about 20% of human LCA cases. A genetic engineering approach was used to cure the disease in these dogs. Normal *RPE65* was engineered into an adeno-associated virus vector and thousands of copies of the genetically engineered virus were injected behind the retina, close to the site where the normal protein is known to function. Ninety-five days after injection, the animals had vision in the treated right eye, judged by pupil response, electroretinogram, and behavioral testing. The investigators showed that transferred DNA persisted in the right eye. The untreated left eye remained blind. A logical question is whether the same approach, subretinal injection of an engineered construct, would also correct blindness in humans with LCA. Safety and efficacy studies are currently proposed as a first step in answering this question.

Crohn's disease (CD) is another area where there have been important advances. Recently, NIH researchers made real progress in understanding the genetic basis of the disease. In a landmark finding, scientists announced the discovery of *Nod2*, the first gene known to confer susceptibility

to CD. Having one mutated copy of the *Nod2* gene doubles a person's chances of developing CD; having two mutated copies (one copy inherited from each parent) can increase the risk 15- to 40-fold.

CD is a debilitating form of inflammatory bowel disease that affects an estimated 500,000 Americans. Most CD patients are young people in their teens and twenties. Symptoms of CD are pain, diarrhea, and rectal bleeding. For decades, the only treatment was surgical removal of regions of the intestine. Current therapy includes oral medication, nutritional supplements, and/or surgery. Development of infliximab (Remicade®), a drug that blocks action of an inflammatory molecule, was a major advance. The medicine alleviates symptoms in two-thirds of patients. Still, two-thirds to three-quarters of Crohn's patients undergo surgery at least once and at least half requires a second operation.

Researchers believe that CD is caused by a combination of genetic and environmental factors. The breakthrough work leading to discovery of a gene for CD used animal models and data from the Human Genome Project. The normal function of *Nod2* is to participate in the immune response to bacteria. The finding that defects in *Nod2* might impair the ability of the normal immune system to respond to bacteria seems counterintuitive, given that CD is thought to arise from an overreaction of the immune system. However, the impaired response of the normal immune system might open the door for an "adaptive" immune response, which could be the source of the disease symptoms. Even though drug treatment (infliximab) is seen as a major advance for CD, scientists want more information about the underlying genetic and environmental causes, because future treatments could be based on this critical knowledge.

Important advances were made in the area of hereditary deafness. Hearing loss affects old and young and can have a number of different causes, including viral and bacterial infection, loud noise, head trauma, exposure to ototoxic chemicals, and genetics. Recently, scientists cloned a gene for inherited Usher syndrome type 1D (USH1D). The gene, located on chromosome 10, codes for a protein called cadherin-23. Children with two mutated copies of the gene (one inherited from each parent) are born profoundly deaf and gradually lose their sight, beginning in adolescence. Studies are underway to understand the function of cadherin-23 in the ear and eye. An understanding of the normal function of the cadherin-23 protein may be a starting point for developing a method to prolong eyesight in children with USH1D.

Another inherited form of deafness is termed DFNB29. Scientists have determined that the gene for this form of hearing deficit is located on chromosome 21. It codes for a protein called claudin 14, which appears to prevent leakage of fluid between cells. Studies using a mouse model are currently underway to clarify the function of claudin 14.

Pendred syndrome is another genetic disorder that is being studied. Children with Pendred syndrome usually suffer profound hearing loss before age three; in addition, they may develop goiters (enlarged thyroid gland) at any age. In recent years the defective gene that causes Pendred syndrome was identified and named *PDS*. The *PDS* gene codes for pendrin protein, which in turn regulates cellular concentration of ions, including iodide, chloride, and bicarbonate.

Scientists have developed a promising genetically-engineered mouse model system to study Pendred syndrome and hearing loss. The mouse was developed with a disrupted *PDS* gene to prevent synthesis of pendrin protein. These mice appear normal at birth but soon develop profound deafness. The observation that the absence of pendrin leads to profound, progressive deterioration of inner ear structures (rather than a developmental defect) suggests a route for therapeutic intervention, which might delay the onset of deafness.

Autism is a developmental disorder that is characterized by a lack of social interaction or responsiveness, limited verbal communication, and ritualized interests and behaviors. Estimates of the rate of autism in the population range from 1 in 2,500 to 1 in 500. The condition appears to involve multiple genes, each having a small effect. Environmental factors play a role in autism, but the genetic component is believed to account for approximately 90% of the condition. Recent work suggests that a chromosomal region containing a gene called *WNT2* may be important in autism. Mouse studies, human genetic studies, and analysis of human DNA support the possibility that this DNA region is implicated in autism.

Most cases of Parkinson's disease do not appear to be inherited. However, in recent years altered forms of three proteins, alpha-synuclein, parkin, and UCH-L1, have been shown to be involved in different forms of inherited Parkinson's. This information provides clues to proteins that may be important in non-inherited Parkinson's. In studies of healthy nerve cells, scientists recently concluded that defects in parkin and alpha-synuclein could result in accumulation of protein aggregates inside the nerve cell and that these aggregates might be harmful to cells in the dopamine pathway. Abnormal aggregation of proteins has emerged as a common theme in neurodegenerative disorders. Developing drugs that interrupt aggregation may be a strategy for slowing disease progression.

Fanconi anemia (FA) is a hereditary disorder that increases risk for some cancers. Although defects in DNA repair are believed to be involved in FA, the molecular mechanism of the disease is not clearly understood. Some FA patients have mutations that affect one of five known FA proteins, but many do not, causing investigators to speculate that another gene may be involved in FA. Recently, researchers identified a new protein, FANCD2 that appears to link the five known FA proteins to the DNA repair machinery. They showed that FANCD2 associates with a known tumor suppressor protein, BRCA1 (a protein implicated in some breast cancers and believed to be important in other diseases as well). They suspect that other DNA repair proteins also associate with FANCD2 and that FANCD2 may turn out to be important in other diseases, in addition to FA.

Interstitial lung diseases are a group of disorders characterized by thickened lung tissue. Some forms of interstitial lung disease appear to run in families, leading scientists to investigate a potential genetic basis of the condition. In normal lungs, the surface of the lung tissue is coated with a mixture of lipids and proteins called "surfactant." Surfactant prevents the lungs from collapsing during normal breathing. It was known that premature infants who lack surfactant have respiratory distress and neonates who cannot produce surfactant B have fatal lung disease. This awareness led researchers to hypothesize that deficient production of surfactant may contribute to interstitial lung disease.

Genetic analysis of a mother and child with symptoms of the disease pointed to a mutation in surfactant protein C. Analysis of lung tissue from mother and child suggested that the protein was not being properly processed and secreted, resulting in lower than normal levels of the protein where it was needed. The study suggests a new etiology (cause) for interstitial lung disease, involving surfactant protein C. The information may eventually lead to new therapies or more effective use of available therapies.

Researchers have learned important information about genes that enhance vaccine action. A vaccine works by priming the immune system so it is prepared for future infection. A common approach to developing a vaccine against a bacterium, virus, or parasite is to identify a specific protein on the infectious microbe, purify it, and inject it as the vaccine. The vaccine itself (the injected material) is not harmful, but it stimulates an immune response that, in theory, will protect the immunized individual, should he be exposed to the intact infectious microbe in the future. A problem is that sometimes the immune response is weak and short-lived.

To improve immunity, vaccines are sometimes injected in combination with adjuvants (substances that enhance the immune response). Recently, scientists discovered that adjuvants act by stimulating a host gene that controls production of Bcl-3 protein. Increasing the level of Bcl-3 protein prolongs the life span of the host immune cells, which translates into an increased immune response to the microbial protein that was injected as a vaccine. This understanding of how adjuvants work at the genetic level furthers an understanding of immune responses. The results of this study may have direct application to the design of new vaccines against infectious agents.

Mouse Models and DNA Microarray Technology

Mouse models. Researchers use information from a number of sources, including the Human Genome Project, to develop relevant mouse models. These models shed light on important human behaviors, metabolic pathways, and diseases. Investigators use mouse models because creating and studying them is relatively straightforward. Researchers manipulate the mouse genome in a variety of ways to create these models, often using transgenic mouse technology. A transgenic mouse is a mouse in which the genome has been altered by introduction of a new gene or a modified version of an existing gene. Using genetic engineering technology, scientists can modify a specific gene in the mouse genome. For example, they can modify the mouse gene so that it is expressed at higher levels; the gene product is said to be overproduced. Sometimes investigators fuse the mouse gene to a gene for another protein, and measure the production of the other protein to get an idea of how the original gene functions.

One of the most valuable approaches is to bring a human gene into the mouse, resulting in what is called a "humanized" mouse. The Working Group commented on the importance of information derived from the Human Genome Project in development of humanized mice. Another widely used and effective strategy is to identify a gene that may be important, engineer a mouse that lacks the gene (a “knockout” mouse), and characterize the effect of deleting the gene. By evaluating what happens to different tissues and organs in the mouse when a gene is knocked out, scientists can begin to understand the role of that particular gene in normal life processes. The Working Group noted that transgenic approaches have provided valuable tools

and information that are highly relevant to human health and disease. The body of knowledge derived from transgenic or knockout mice seems to be increasing at an almost exponential rate.

Obesity is one component of a "metabolic syndrome" that also includes diabetes, hypertension, dyslipidemia, and cardiovascular disease. Metabolic syndrome is believed to result from the interaction of abdominal fat, total body fat, and insulin resistance. Obesity appears to be influenced by multiple genes and their interaction with the environment. Recent studies have linked obesity with regions on chromosome 10, chromosome 3, and chromosome 17. Researchers are studying some of the genes known to be present on these regions; further work on these candidate genes and their protein products will contribute more information toward understanding the mechanism of obesity and the dangerous condition known as metabolic syndrome.

Diabetes research has greatly benefited from studies using mouse models. By studying genetically engineered mice, researchers have developed an arsenal of information about hormonal regulation of eating, body composition, obesity, and insulin resistance. Researchers found that melanin-concentrating hormone (MCH) appears to stimulate eating. Mice that were engineered to overproduce MCH are insulin-resistant, the hallmark of type 2 diabetes. Mice that lack insulin receptors in the brain also show signs of type 2 diabetes, including insulin resistance and high blood glucose. Researchers found that deletion of the GLUT4 gene caused insulin resistance. Similarly, they found that deletion of the Akt2 gene results in impaired glucose tolerance, a pre-diabetic condition.

The hormone leptin acts with its receptor to send the brain a signal that enough food has been eaten. Mice that lack the leptin receptor are obese, apparently because they don't know when to stop eating. By constructing and studying mouse models, scientists are uncovering a complex system of signaling pathways. Understanding how these signals interact and how the brain receives them is expected to reveal avenues for treatment of obesity, insulin resistance, and diabetes.

Mouse models are being used to study drug-taking behavior. Experiments with transgenic mice demonstrated the importance of DfosB, Cdk5, and DARPP-32 proteins in mediating the effect of cocaine on the brain. These chemicals were important during the transition from voluntary cocaine use to addiction. The mouse studies reveal a cascade of cellular events that occur in the brain and are related to cocaine addiction. Understanding these processes will be key in developing treatments for drug addiction.

Leukodystrophies are a group of disorders characterized by degeneration of the insulating material that covers nerve fibers (white matter). Scientists created genetically engineered mice to study one such leukodystrophy, Alexander disease. They developed mice that overproduce the protein GFAP (glial fibrillary acidic protein), a critical component of the structure of a type of cell called astrocytes. Researchers found that there were protein aggregates inside the brains of these genetically engineered mice that were similar to protein aggregates found in brain cells of children who die of Alexander disease. The findings provide a clue to what goes wrong in Alexander disease and the model will help scientists test strategies to stop the process.

DNA microarray technology. DNA microarray (gene chip) technology is used to obtain a snapshot of gene activity in a cell or tissue. Scientists use microarray to test the activity of thousands of genes at the same time. Using DNA microarray technology, scientists can tell which genes are active (expressed) in a cell or tissue at a given point in time. The technology is used to monitor activities of healthy cells and to characterize tumors and tumor cells.

Scientists know that mutations in the BRCA1 and BRCA2 genes are a major cause of hereditary breast cancer. Differentiating between hereditary and non-hereditary breast cancer was not easy using traditional techniques. Recently, scientists used microarray technology to look at tumor DNA and were able to quickly and accurately differentiate between tumors arising in women with BRCA1, BRCA2, and non-hereditary cases. The DNA microarray technique should make it possible to quickly and accurately diagnose the cause of a tumor and may ultimately guide decisions about treatment.

Four different childhood cancers (neuroblastoma, rhabdomyosarcoma, non-Hodgkin lymphoma, and Ewing family of tumors) constitute a group of cancers that appear very similar under a microscope. In contrast, the treatment options, response to therapy, and prognoses of these cancers vary widely, making it essential that the diagnosis is accurate. Recently, scientists developed a method of analysis that can differentiate between these closely related types of childhood cancer. The method relies on DNA microarrays and a form of artificial intelligence called an artificial neural network (ANN). ANN analyzes the enormous amount of data generated by the microarrays and makes a highly accurate diagnosis. In addition to providing an accurate diagnosis of the cancer type, this approach identified 41 new genes that may provide important insights into cancer biology and may ultimately be therapeutic targets.

New Therapeutics Targets

The Working Group was impressed with the number of reports that provided information on basic biological processes and at the same time, pointed towards avenues of investigation that could lead to new therapies or treatment approaches.

Alzheimer's. This disease is characterized by amyloid-β plaques in the brain and by the presence of neurofibrillary tangles in certain brain regions. The apparently harmful amyloid-β plaques result from deposition of amyloid-β peptides. Many scientists believe that the deposition of amyloid-β peptides starts the degeneration cascade of Alzheimer's disease.

The amyloid-β peptide is formed when it is clipped off from a larger protein called amyloid precursor protein. The amyloid-β peptide fragment does not form a plaque until it is clipped from the larger protein. Recently, scientists identified an enzyme, β-secretase (BACE), that helps clip the amyloid-β peptide from the larger protein. There are two forms of the β-secretase enzyme, called BACE1 and BACE2.

Using cell culture and transgenic knockout mouse experiments, scientists identified BACE1 as the brain enzyme that plays a key role in formation of amyloid-β plaques. The knowledge that BACE1 is the principal enzyme in this process makes it a likely therapeutic target and an

appropriate focus for the design of pharmacologic drugs that would inhibit its function. Work is currently being done to develop pharmacological drugs that act as BACE1 inhibitors. The aim is to develop drugs that interfere with formation of amyloid-β peptides and thus possibly prevent, delay onset, or reduce the severity of Alzheimer's disease.

Illnesses induced by hypoxia. How cells sense changes in oxygen availability is a fundamental question in medicine and cell biology. Chronic lack of oxygen (hypoxia) is associated with many disease states, including tumor progression, ischemic brain and heart, stroke, cardiac arrest, pulmonary disease, and anemia. In addition, some fetal maladies result from hypoxia.

In mammals, hypoxia stabilizes a cellular factor (hypoxia-inducible factor, HIF) that may cause some of the deleterious effects of hypoxia. Recently, researchers further elucidated the oxygen sensing pathway by identifying a mammalian enzyme that regulates this factor. This finding is relevant to a number of diseases. It may be possible to develop drugs that target oxygen-sensing and oxygen-signaling pathways. Such drugs could be useful in treating a wide range of diseases, such as stroke, heart attack, and solid tumors.

Damage caused by reoxygenation after hypoxia. When the blood vessels and heart are denied oxygen, cellular damage occurs. Paradoxically, when the blockage is removed, additional local damage occurs. This type of hypoxia-reoxygenation injury occurs when patients undergo a variety of treatments and surgeries, such as balloon angioplasty, reconstructive plastic surgery that relies on using a patient's skin tissue to create flaps, and re-attachment of extremities. Because it is often medically necessary to correct oxygen-poor conditions in the body, scientists are very interested in understanding the underlying mechanism of the hypoxia-reoxygenation process and identifying ways to prevent reoxygenation injury.

Using cells derived from cow aorta (a large artery that is connected to the heart), researchers observed that cells undergoing hypoxia followed by reoxygenation had reduced levels of a particular protein, CYP2J2. CYP2J2 is an enzyme that is responsible for producing other compounds, called EETs. The researchers found they were able to prevent reoxygenation injury in cultured cells by maintaining levels of CYP2J2, adding more EETs, or preventing the breakdown of EETs. These findings provide clues for development of possible therapeutic interventions to prevent hypoxia-reoxygenation injury to patients during medical and surgical procedures.

Hepatitis C. Most individuals infected with the hepatitis C virus (HCV) develop chronic liver disease, cirrhosis, or liver cancer. HCV is a widespread disease that kills up to 10,000 Americans each year. HCV causes disease by invading a mammalian cell and using the cell's own protein-making apparatus, the ribosome, to synthesize viral proteins. The viral proteins are used to make more virus particles, which increase the number of virus particles inside the cell and ultimately causes the host cell to break open. This, in turn, facilitates spread of newly formed virus particles to other cells.

Recently, scientists used cryo-electron microscopy to capture the first image of HCV genetic material (RNA) bound to the ribosome of a host cell. The image revealed that the end of the HCV, RNA twists into a hook that snags the host ribosome and dramatically changes its shape.

The snagged ribosome is unable to function normally to synthesize host proteins and is able to generate only viral proteins. By providing a clear view of how the infecting virus takes over the protein synthetic machinery of the host, this work may point to new molecular targets for pharmacological drugs that act against HCV. In addition, other viruses, such as those associated herpes, foot-and-mouth disease, and polio, are thought to use similar infection strategies, and this information about HCV may also advance efforts to design drugs to treat other viruses.

In another study, scientists observed that when a particular region of the HCV genome is mutated (the region that codes for the NS5A protein), the HCV virus replicates more efficiently. They exploited this discovery to develop a new cell culture system that will be used to study HCV replication. The identification of mutations in the NS5A region, which appear to affect replication, may aid in development of an HCV-attenuated vaccine (a vaccine containing a weakened virus that normally does not cause disease but triggers an immune response that protects against the disease-causing form of the virus).

Cholesterol transport. High-density lipoprotein (HDL) is often termed "good" cholesterol. While studying Tangier disease, a rare condition characterized by a lack of HDL, researchers uncovered information that is relevant to more widespread conditions involving coronary artery disease. It was known that the ABCA1 protein is necessary for HDL formation. The Tangier disease study used transgenic mice that were engineered to have higher levels of ABCA1 protein. Investigators found that the mice with high levels of ABCA1 protein had higher than normal amounts of "good" cholesterol in their blood and that the animals excreted cholesterol at a higher rate than normal animals.

In a separate study, researchers characterized several steps in ABCA1 production and demonstrated that if ABCA1 was not allowed to localize to its normal place in the cell membrane, removal of intracellular cholesterol was impaired. The observation that increasing ABCA1 increases both HDL levels and cholesterol excretion supports use of ABCA1 as part of a pharmacological approach to treating cardiovascular disease in the future. Understanding the steps of ABCA1 production and localization provides additional information that could be useful in development of new pharmacological drugs. The fact that information that may be widely applicable to heart disease came out of a study of Tangier disease illustrates a benefit of studying rare diseases.

Osteoporosis. Bone tissue is dynamic, and bone breakdown (resorption) happens normally as part of bone remodeling, the process by which old or damaged bone is replaced with new bone. Osteoporosis occurs when bone resorption exceeds bone formation and there is a net loss of bone tissue. It is known that the female hormone estrogen prevents bone loss and that bone loss frequently occurs in post-menopausal women who have reduced estrogen levels.

Recently, scientists found that estrogen prevents bone loss by decreasing the rate of programmed cell death (apoptosis) among bone-forming cells (osteoblasts), thus enhancing bone formation. In addition, it was found that the male hormone androgen also has an anti-apoptotic effect on bone-forming cells and could prevent net bone loss. Both estrogen and androgen act on cells through mediator proteins, called receptors. The effect of estrogen and androgen on bone can be mediated by either estrogen receptors or androgen receptors, regardless of which sex hormone is present. It

appears that these effects of sex hormones on bone reflect a previously unrecognized function of the estrogen and androgen receptors, which is distinct from their familiar action on reproductive tissues. This new information on the ability of estrogen and androgen to decrease the death rate of bone-forming cells may reveal additional targets for development of pharmacologic drugs to prevent or treat osteoporosis.

Osteoarthritis. Osteoarthritis (OA) is the most widespread form of joint disease and a common cause of pain and disability in older adults. OA is characterized by loss of cartilage accompanied by local enlargement of bone tissue. Epidemiological studies suggest that estrogen may be protective against OA, but the biochemical mechanism for this protection is not yet understood. Recently, investigators used cynomolgus monkeys to study development of OA in aging animals and as a function of surgically induced menopause. The study revealed an age-related decline in the response of cartilage cells to a protein called insulin-like growth factor 1 (IGF-1). The study also revealed that giving estrogen replacement to animals after surgically induced menopause affected their cartilage metabolism. These findings could contribute to a storehouse of information upon which to base OA drug development.

Drug-resistant malaria. Malaria strikes an estimated 300 to 500 million people a year and kills more than one million of them. The heaviest toll is among children in sub-Saharan Africa. The disease is caused by infection with the single cell parasite, *Plasmodium*, transmitted by the bite of mosquitoes. Chloroquine has been an effective treatment for malaria, but treatment of the disease with chloroquine was set back by the emergence of chloroquine-resistant strains of *Plasmodium falciparum*, the most deadly species of malaria parasite. Chloroquine resistance appeared in Southeast Asia and South America in the late 1950's and in Africa in the late 1970's.

For a number of years NIH researchers have been working to understand the mechanism of chloroquine resistance. Recently, a combination of laboratory, clinical, and field work culminated in the knowledge that genetic mutations in *P. falciparum*, including the *pfcrt* T76 mutation, are responsible for chloroquine resistance. There was also a link between chloroquine resistance and another *P. falciparum* mutation, *pfmdr* 1. This knowledge of the genetic mutations that confer drug resistance to parasites could provide guiding principles in a strategy to develop a modified form of chloroquine that has renewed effectiveness against the drug resistant parasite.

Sleeping sickness. The parasite *Trypanosoma brucei* causes sleeping sickness (trypanosomiasis), a disease that is fatal to humans and livestock. The parasite, which feeds on blood, is transmitted by the bite of the tsetse fly. Like many parasites, *T. brucei* has a complex life cycle; the organism can survive inside both flies and mammals, two environments where conditions are very different. Recently, scientists identified a *T. brucei* enzyme that the parasite depends on for survival in the mammalian bloodstream. That enzyme is a form of RNA ligase. Scientists discovered they could thwart the growth of the bloodstream form of *T. brucei* by eliminating this enzyme. By demonstrating that this *T. brucei* RNA ligase enzyme is essential for survival of the parasite in the bloodstream, the investigators have identified a potential target for a pharmacological drug to treat sleeping sickness. Presumably, a drug that could degrade the RNA ligase or inhibit its function would fight trypanosomiasis.

Structural Biology

There have been tremendous advances in the ability of scientists to analyze protein structures. A common approach to determining the structure of a molecule is to induce it to form crystals and to determine the shape of the crystal. The investigator determines the shape of the crystal by bombarding it with X-rays and analyzing the pattern that the X-rays make when they bounce off the crystal. Investigators are able to deduce the structures of increasingly complex proteins because they have learned how to form crystals of proteins that were previously believed impossible to crystallize. The field has progressed so that now investigators are able to crystallize proteins with mutations in critical regions and understand how the mutations alter protein function.

Three-dimensional structure of a key enzyme in life processes. RNA polymerase II (Pol II) is the enzyme responsible for the first step in protein synthesis in organisms ranging from yeast to humans. Pol II is a 12-subunit entity that forms a complex with DNA. It is a molecular machine that reads the genes present on DNA and transcribes that information into RNA messages. After the RNA messages are released from Pol II they are translated into protein.

After nearly 20 years of effort, structural biologists succeeded in using X-ray crystallography to elucidate the three-dimensional structure of Pol II. The investigators determined the shape of the 12-subunit enzyme in two states: an open conformation (or shape) and a partly closed conformation. These conformations differ in the position of a section of the enzyme called the clamp, which is the part of Pol II that is thought to close over the DNA. The enzyme is a dynamic structure that changes shape as it functions, moving into and out of the two conformations (and probably other conformations, as well).

In addition to determining the shape of open and partly closed conformations of Pol II, investigators have elucidated the shape of a complex that contains the enzyme and DNA. This third crystal structure captures a freeze-frame "picture" of the enzyme in the process of reading the DNA and producing the RNA message.

Although obtaining the crystal structure of Pol II is an end in itself, it is also part of a wider quest to understand transcription. The solved structure gives scientists their first look at the enzyme in action. It suggests a role for each of the subunits and reveals how they fit together to form a molecular machine that copies genes into RNA. This work may ultimately have clinical applications. Researchers may be able to design new antibiotics by targeting structural differences between human and bacterial forms of RNA polymerase. They may be able to design anti-cancer drugs that prevent Pol II from stimulating cell growth in tumor cells.

Insulin receptor. Insulin is a hormone that stimulates cells to remove glucose from the blood. Insulin acts by binding to the insulin receptors that are on the surface of some cells. Type 2 diabetes, characterized by insulin resistance, often results from malfunctioning insulin receptors.

Currently, studies are underway to determine how the receptor functions. Some scientists are analyzing fragments of the insulin receptor, rather than the receptor as a whole. These studies provide mechanistic information about the intracellular region of the receptor.

Aging

Advances in aging research include new information about the molecular basis of longevity as well as demographic information relating to quality of life.

It has been known for a long time that a diet rich in nutrients but extremely reduced in calories (30% less than normal) increases the life span of rats and mice. However, for quality-of-life reasons, most people are not willing to restrict calories to that extent. Still, there is a lot of interest in the underlying mechanisms of life extension.

Scientists recently identified two genes that affect longevity in fruit flies. One of these fruit fly genes codes for an enzyme that affects mitochondrial metabolism, ATP, and reactive oxygen species. The other fruit fly mutation reduces activity of the insulin-like signaling pathway. Other findings using nematodes (worms) and mice are consistent with the insulin-like signaling pathway affecting life span.

These genetic mutations in mitochondrial metabolism and insulin-like signaling may have the same effect on worms, flies, and mice as caloric restriction does in rodents. The finding that insulin-like signaling affects aging in organisms ranging from worms to flies to mice raises the interesting question of whether the same pathway might play a role in human aging.

Production of human growth hormone decreases with age. A study performed a decade ago showed that weekly injections of growth hormone increased lean body mass and decreased fat tissue. Based on this, some doctors have recommended growth hormone injections as an anti-aging treatment for elderly patients. This approach is not supported by a recent mouse study. Scientists showed that a strain of mice that are unable to produce growth hormone because of a genetic mutation live 30-40% longer than normal mice. The mutant mice have higher than normal levels of anti-oxidant enzymes, reduced blood glucose, and increased sensitivity to insulin. They are smaller than normal mice and are called "dwarf" mice. Several age-sensitive measures of immune system status and age-dependent changes in connective tissue are delayed in these mice. The mice are deficient in other hormones but experiments suggest it is the growth hormone deficiency that is responsible for the delayed aging. The data provide insight into hormonal regulation of aging and suggest a need to reconsider the wisdom of long-term injection of growth hormone in humans as a desirable intervention to slow down or reverse aging.

Maximum age at death -- human studies. Analysis of Swedish national demographic data collected from 1861 to 1999 showed that the maximum age at death rose from 101 years to 108 years. Most of the increase (more than 70%) reflects better survival of individuals who have reached age 70. The study used data from Sweden because a large data set spanning a long time period was available. It seems likely that these results apply to other industrialized countries, including the United States.

Decline in disability among older Americans. The 1999 National Long Term Care Survey indicates that the rate of disability among older Americans has declined over the past two decades. There were 7 million chronically disabled Americans in 1999, which is 2.3 million

fewer that there would have been had the rates not changed since 1982. The reduction in disability rate was greater for older black Americans than for the population as a whole. Similar trends were seen in other studies (Survey of Income and Program Participation, Medicare Current Beneficiary Survey, National Health Information Survey) over the same or nearly the same time period.

A study called Instrumental Activities of Daily Living suggests that fewer older people are having difficulty with routine care activities such as household chores and errands, although the number who have severe personal care disability (e.g., difficulty with bathing, dressing, and eating) has not changed. Analysis of data from the Health and Retirement Study indicates that severe cognitive impairment in older Americans declined from 6% in 1993 to 4% in 1998.

Researchers believe that a decline in disability reflects improvements in physiological health, better therapies, and improved coping strategies. Efforts are underway to understand long-term economic consequences of the decline in disability.

Caregiving research. While some of the care for older people is provided by home health agencies or nursing homes, much of it is provided informally at home by family and friends. In 1997, the economic impact of informal caregiving was estimated at $196 billion, compared to $32 billion for home health care and $83 billion for nursing home care. Many informal home caregivers deal with complex and demanding care requirements. NIH studies have contributed to increased understanding of stressors and predictors of bad outcomes, and have identified predictors of family dynamics that are responsive to interventions. Maintaining the health of the care providers as well as the care recipient is considered crucial to successful informal home care. Currently funded work is investigating how to encourage caregivers to reach out and obtain services and support that might be helpful to them.

Behavior and Neuroscience

In the area of neuroscience, investigators continue to use a variety of tools, including sophisticated imaging techniques and animal models, to explain the molecular basis of complex behaviors.

It has been known for some time that drugs of abuse (cocaine, heroin, methamphetamine, nicotine) cause brain levels of the neurotransmitter dopamine to increase in brain regions associated with reward and reinforcement. Now, two studies using neuroimaging technologies suggest that some of the same mechanisms are involved in gambling and obesity. Sophisticated neuroimaging techniques were used to monitor brain activity of human subjects while they engaged in gambling and eating. The studies revealed that some of the same brain circuits are involved in gambling and eating that are involved in drug use.

In another study, researchers used functional magnetic resonance imaging (fMRI) to look at brain regions that are activated when a cocaine user experiences a craving. The study showed that the region activated when the drug craving occurs is the same region that is activated in a non-drug user's brain by sexual stimuli (a sex film). In addition, the sex film did not activate the drug users' brains as much as it activated the non-drug users' brains. This suggests that cocaine

craving not only acts on the brain's rewards circuits, it changes the user's normal emotional responses to certain stimuli, such as sex. This could explain the changes in judgment and priorities that a long-term drug-user typically exhibits.

MDMA (3,4-methylenedioxymethamphetamine) is a drug of abuse known as "Ecstasy." Recently, scientists using a rat model showed that MDMA causes memory loss and learning deficiencies when animals are exposed to the drug during the period when the central nervous system is developing. In rats, this period is days 1-10 and 11-20 of the neonatal period. These developmental periods correspond to the early and late third trimester in humans. This study is important because young adults continue to use MDMA, and many of them harbor the false notion that the drug as a benign substance. In reality, Ecstasy use by a pregnant woman is harmful to the developing fetus.

Investigators want to understand the transition that occurs when a person goes from being a voluntary user of a drug to a compulsive drug user, or addict. Using a rodent model, investigators found that a single dose of cocaine can change brain physiology in the area of the brain known as the ventral tegmental area (VTA), a region that is involved in learning and memory. An understanding of these changes in the brain may provide information about the early stages of addiction.

In another study, investigators studied the neurobiology of relapse. They wanted to understand how in humans, environmental cues (such as a social situation or location) can bring back memories of being high and trigger a relapse into drug-taking behavior. It was known that relapse is connected to memory and that the process involves a brain region called the hippocampus. Using a rat model, the investigators determined that the section of the hippocampus known as the ventral subiculum is implicated in drug relapse. This section of the brain is involved in memory and is rich in the neurotransmitter glutamate. When cocaine-addicted rats were treated with a pharmacological compound that blocks the action of glutamate, they did not experience relapse. This finding suggests that agents that block glutamate may be useful as a medication to prevent memory-associated or environmental cue-induced relapse.

Verification/Validation of Performance Measures and Data Issues

NIH's progress toward meeting this goal has been assessed by a working group of the Advisory Committee to the Director (ACD), NIH. The GPRA Assessment Working Group was composed of members of the ACD, the NIH's Council of Public Representatives (COPR), and selected members of the Institute and Center (IC) national advisory councils.

The assessment of NIH's research was based on data provided by the ICs (science advances, science capsules, and stories of discovery, as well as research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. Key references were provided for all science advances, science capsules, and stories of discovery. NIH also provided copies of full articles to the assessment working group whenever requested.

(For a further discussion of this assessment process and the members of the Working Group, see Appendix 1).

The criteria that were developed and used to assess the outcomes of NIH research under goal a in FY 2001 are as follows:

The NIH biomedical research enterprise *has successfully met this goal* when its research yields new findings related to biological functions and behavior, and the new findings are published and/or disseminated.

The NIH biomedical research enterprise *has substantially exceeded this goal* when, in addition to fulfilling the criteria under *successfully met*, any of the following applies:

- Discoveries result in significant new understanding of a particular biologic or behavioral process. Such new understanding may open up new avenues of research or be applicable to other disciplines, other areas of research, or other diseases.

- Research yields answers to long-standing, important biological and behavioral questions, or provides novel investigative approaches for addressing such questions.

- Genomic information about humans, model organisms, and/or disease-causing agent is translated into new understanding of the role of genes and/or environment in human health, disease, and behavior.

- Discoveries have potential for translation into new or improved technologies, diagnostics, treatments, and preventive strategies.

The NIH biomedical research enterprise *has not met this goal* when its research fails to yield new findings related biological functions and behavior, or when new findings are not published and/or disseminated.

Goal b) Develop new or improved instruments and technologies for use in research and medicine.

The development of new or improved instruments and technologies has always played a complementary and critical role in the success of biomedical research. The dawn of the 21st century finds biomedical research increasingly more complex and multi-disciplinary. As the result, researchers face the constant challenge of finding new and more effective ways to probe these complex systems. Only then, can important information be translated to knowledge and ultimately, converted into effective prevention, diagnosis, and treatment of diseases for mankind. Unlike a century ago, this effort requires collaborations between and among scientists from a wide range of disciplines, including chemistry, biology, genetics, mathematics, computer science, engineering, and physics. Nowhere is this more evident than the ever expanding field of genomics–the collection and analysis of genetic information. This year, new and improved instruments and technologies have further allowed scientists to apply this vast amount of data toward understanding and treating various diseases. This same trend also extends to other areas of research involving instruments and technologies.

In many cases, advances in instrumentation continue to be built on previous research. One good example is found in the area of imaging. Imaging techniques have continued to be fine-tuned and become more sophisticated, greatly aiding our ability to understand complex systems such as the visual and central nervous systems. Traditional tool such as electron microscopy has also been improved to give images with much greater resolution–allowing live detailed observation, in some cases, of complex cellular processes.

In other cases, instrumental techniques, which traditionally have not been widely used in biomedical research, have found new audiences. For example, mass spectrometry–widely used in chemistry and physics–is now being modified to find drug targets, analyze cocaine exposure in newborns, and separate complex proteins. Other spectroscopic techniques such as X-ray crystallography now gives better 3-dimensional molecular details of large, complex proteins more than ever.

Microarray techniques have continued play a key role in the area of instrumentation. It has revolutionized the speed and efficiency with which scientists can analyze genomic data. New and improved databases have been developed for storing, compiling, and analyzing the vast amount of microarray data. The ability to analyze many genes simultaneously allows scientists to compare and characterize genes involved not only in a variety of genetic disorders, but also those important to the developmental and aging processes.

In the area of information technology, the refinement of databases has allowed researchers to better classify and predict 3-dimensional protein structures based on their amino acid sequences. A firm grasp of the structures of proteins is the key to understanding root causes of diseases. Innovative algorithm development has also played a key role in producing effective models for monitoring specific disease stages. It helps monitor DNA changes in tumors, improves colon

cancer detection, and predicts survival rate of end-stage liver disease, to name just a few examples. In another related area, improved statistical analysis of various clinical studies has led to better data interpretation, evaluation, and identification of fundamental causes of serious epidemics.

This year has witnessed an explosion in cutting edge biological tool development, which provides scientists invaluable insight into molecular mechanisms of diseases. One area at the forefront of this development is transgenic technology. This innovative technology–where specific genes can be added to or subtracted from animals' genomes–provides critical models for devastating human diseases such as Alzheimer's and Parkinson's diseases.

Indeed, two long-time NIH-supported scientists were honored this year with the prestigious Albert Lasker Award for their pioneering work with transgenic mice. Another area of focus is cell and gene therapy, which involves the isolation, purification, and characterization of various donor sources, including stem cells. Alternative means involving tissue repair and engineering continue to be explored to treat difficult problems such as wound healing. Much effort has also gone into the development of techniques and devices to effectively deliver donor cells to their target sites.

For fiscal years 1999-2001, NIH measured its success under this goal against the broad target of progress in developing new instrumentation or technologies that enhance capabilities for investigating biological functions and diagnosing and treating diseases and disorders. For fiscal years 2002 and 2003, NIH has put in place two representative subgoals to better define NIH's research plans under this goal. These subgoals focus on developing new technologies to enable greater understanding of genomic and proteomic information, and on developing biocompatible materials for use in replace or repairing damaged and non-functioning or missing tissue. The importance of these subgoals is detailed below.

Subgoal b.1. Develop new technologies to enable greater understanding of genomic and proteomic information.

Before the advent of current technologies, the study of a single protein could justifiably occupy a researcher's entire career. Arguably heroic efforts had to be made to determine the structure, function, kinetics, tissue location, and other characteristics important for understanding the protein's role in the body. Mapping a protein to a gene could require years of intense, collaborative work. Ultimately, the earlier, reductionist approach sought to understand how a single protein operated in both normal and abnormal biology, despite an awareness that the cell consists of and is influenced by thousands of other proteins. Simply put, twentieth century researchers simply did not have the data or the tools to simultaneously study the roles of many proteins interacting within the network between and within cells. Twenty-first century researchers are asked to do just that.

As quickly as the development of bioinformatics platforms has progressed, deriving a real understanding of genomic and proteomic information will necessitate the development of new applications for the interpretation of these data. It is now recognized that modification occurs to proteins that are not encoded for by the genome, resulting in the existence of multiple forms of

proteins that influence cell function. Thus, understanding the human proteome is less of a cataloging of gene expression than an investigation of mechanisms of diversity. Clearly, databases must be developed to encompass the wealth of information, and new technologies must arise to support continued advances. In particular, if the disciplines of pharmacokinetics and pharmacodynamics (PK/PD) are to benefit from the information explosion resulting from the Human Genome Project, new tools are needed to access that information and make it available for drug development. If genechip technology and microarray expression data are to be useful for biomedical research, novel biostatistical analysis and data integration tools must be developed. If individualized medicine is to become a reality, artificial intelligence-based bioinformatics programs must be able to assimilate various forms of basic and clinical data, interpret those data, and make intelligent suggestions. It will be critical that these suggestions be based on appropriate information, and that means on data from age-, sex-, gender-, and race-matched studies, as well as on single nucleotide polymorphism (SNP) databases, case history data, clinical trial results, and multiple sources of raw data. The challenges for maximizing the use of genomics and proteomics data are weighty, but they are not insurmountable, and these are the tasks laid upon researchers in this subgoal.

Subgoal b.2. Develop biocompatible materials for use in replacing or repairing damaged and non-functioning or missing tissue.

The development of biocompatible materials is in the domain of biomedical engineering – a field that paradoxically requires its researchers to be experts in a broad range of scientific disciplines. The replacement of living tissue with man-made materials demands an in-depth understanding of the physical sciences – chemistry, physics, and mathematics – as well as of the biological sciences including anatomy and physiology, biochemistry, immunology, hematology, neurology, and often surgery. To repair or replace damaged and non-functioning or even missing tissue, materials are designed, tested, modified, and screened again for their ability to avoid or withstand the sheer forces encountered in the circulatory system, the friction and pressure requirements of load-bearing joints, and the keen discernment and persevering attacks of the immune system trying to rid the body of foreign objects.

As much as the field of biomedical engineering has progressed in recent years, including the manufacture, implantation, and medical success in the past year of a fully encased and internal artificial heart, the challenges yet facing researchers are myriad and difficult. Basic research is still needed in the area of tissue compatibility. The discipline of materials science must continue its efforts in matching the strength, weight, and elasticity requirements of second and third generation prosthetics. Inducing rapid skin and artificial skin engraftment, minimizing scarring, and preventing pain, infections, and shock in burn victims and cancer surgery patients remain constant challenges for researchers in this field. Whether tissue must be repaired because of birth defects or trauma, replaced because of age or disease, or emplaced because of genetic abnormalities, there must be more research into the basic and clinical sciences supporting the diverse disciplines that are integrated in the expertise of researchers confronting the challenge of developing novel biocompatible materials.

Annual Performance	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Progress in developing new instrumentation or technologies that enhance capabilities for investigating biological functions and diagnosing and treating diseases and disorders.	★	★	★		
b.1. Develop new technologies to enable greater understanding of genomic and proteomic information.					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇
b.2. Develop biocompatible materials for use in replacing or repairing damaged and non-functioning or missing tissue.					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇

★ Target Substantially Exceeded	◆ Target Successfully Met	◇ Target Active	✖ Target Not Met

Summary of Performance Results

- **New or improved instruments/technologies, as well as new applications of existing instruments/technologies, are enabling researchers to answer important biological questions relevant to human health.** The NIH's institutes and centers submitted 87 science advances, science capsules, and stories of discovery (tabulated at the end of this section) under goal b for FY2001. In the judgment of the assessment working group, the NIH has "substantially" exceeded its target in developing new or improved instruments and technologies for use in research and medicine (see *Performance Assessment Approach* criteria above for "substantially exceeding" goal).

  Some members commented on the interconnectedness between goal b and three other goals– diagnosis, prevention, and treatment. The consensus was that new or improved instruments and technologies in FY 2001 not only offered insight into important and fundamental biological processes, but they also paved the way for better diagnostic, preventive, and treatment of human diseases.

  Some of these technologies continue to be built upon advances from FY 2000. One prominent example is the use of microarray technology to analyze gene activity of thousands of genes simultaneously to identify those implicated in cancers and other genetic disorders. Another advance that was deemed significant was in the area of communications. NIH was able to use information technologies effectively to provide scientific data to a wider audience of researchers, as well as health information to the general public.

  In FY 2000, the Assessment Working Group noted that the vast majority of these scientific advances were "high risk" projects meaning that the likelihood of success could not be guaranteed but that impact would likely have high payoffs in the form of breakthroughs, paradigm shifts, and expanded scientific applications. Members of the Working Group

collectively confirmed that knowledge gained from the use of these instruments/technologies will foster the development of new and improved diagnostics, treatments, and preventive strategies that will ultimately improve human health and well-being.

In FY 1999, the Assessment Working Group determined that research outcomes have significantly contributed to progress in developing new or improved instruments and technologies. The new or improved instruments/technologies, as well as new applications of existing instruments/technologies, are enabling researchers to answer important biological questions. Knowledge gained from the use of these instruments/technologies will underpin the development of new and improved diagnostics, treatments, and preventive strategies that will ultimately improve human health and quality of life. In their discussion, members of the Working Group identified a number of important themes or categories of research outcomes, discussed the significance of these types of findings, and highlighted a number of research outcomes that they judged to be especially noteworthy.

Research Outcomes and Their Significance

The assessment working group highlighted a number of significant research outcomes that substantially exceeded the assessment criteria for goal b. Several research themes emerged from the discussion and they are described in some details below.

Microarray Technologies

Microarray technologies continue to provide powerful tools for understanding complex diseases, something that previously was not possible. The ability to screen many genes at once and analyze their expression–instructions to make specific proteins–allows researchers to profile genes in both normal and diseased states. These profile markers, in turn, improve diagnostic prediction and help find optimal treatment strategies for individual patients.

In the case of pulmonary hypertension (PPH)–a fatal lung disease–rapid microarray screening revealed that over 300 genes were expressed differently in lungs of PPH patients. Furthermore, it revealed two distinctly different gene expression patterns, depending on the type of PPH, sporadic or familial. The ability to distinguish sporadic, which displays similar genetic mutations as cancer, from familial PPH has profound implications for the development of treatments for PPH patients.

Gene microarray analysis is also advantageous in identifying specific diseased states. Analysis of 11,000 genes in gliomas (most common brain tumors) of different grades enabled researchers to narrow it down to 14 genes that are overexpressed in aggressive gliomas. These 14 genes could further be pinpointed to 2 broad groups: one related to growth factor and one related to extracellular matrix structure. This type of specific information provides not only important clues to why tumors develop and progress, but also provides new therapeutic targets for treatment.

Databases and Software Developments

Microarray technology is being used to provide answers to fundamental questions such as, how do genes control cell and tissue function? In this regard, it is a good vehicle for establishing large DNA databases for characterization and functional classification of a large collection of genes. These databases potentially can offer scientists worldwide a convenient way to study genes implicated in many important biological functions.

One such significant advance is the development of 15,000 mouse genes, called the "NIA mouse 15K cloned gene set", with emphasis on genes active in aging and in placental and embryonic developments. This collection of genes has been distributed freely to over 100 research institutions worldwide, whose research has resulted in the identification of over 4,000 genes involved in numerous biologically important functions: cell death (apoptosis), cell cycle, matrix/structural proteins, energy/metabolism, DNA transcription/replication, protein synthesis, signal transduction, etc.

Another useful DNA database was established for the South African clawed frog (*Xenopus laevis*)–an important model organism for human development and disease. DNA sequences generated and characterized from unfertilized *Xenopus* eggs represent genetic contributions to early development. The knowledge of early development-related genes help aid, for example, toxicology studies–allowing researchers to evaluate subtle environmental effects on development.

NIH has also made significant strides toward developing supporting tools for managing and interpreting microarray information. MAPS (Microarray Project System) is a good example of a functional database that is designed to store, compile, and analyze gene expression data. It features a convenient web interface to DNA microarray information, validates replicate gene expression results, and queries gene expression data based on gene classifications of interest.

New or improved computer and software programs have also had a large impact on data interpretation. One noteworthy example is the development of a "tree" model to analyze tumor DNA data. This mathematical model is used to analyze chromosomal mutations in tumors and allows researchers to predict genes responsible for tumor initiation and progression. The ability to monitor tumor progression is crucial to controlling and preventing the many different forms of cancer.

Another substantial advance was the development of a computer algorithm to analyze computed tomography (CT) scans for colonic polyps (small growths in the wall of the colon). This algorithm creates a three-dimensional model of the patient's colon–allowing the computer to inspect hundreds of thousands of points on the model for protrusions. This "virtual colonoscopy" technique enables physicians to detect polyps more effectively and in a less intrusive manner to patients.

Tools for Probing Protein Structures

Important advances were made in providing tools for understanding complex proteins. An outstanding advance in this area was the *Clinical Proteomics Initiative*–created in collaboration with the FDA. This initiative successfully developed technologies to screen both blood and tissue samples of patients inflicted with various forms of cancer (prostate, breast, colon, etc.).

Two major technologies developed from this initiative are laser capture microdissection and protein microarrays. Laser capture microdissection makes it possible to isolate pure cells from tissue samples. Protein microarrays, on the other hand, allows scientists to profile the state of key proteins in signaling pathways. The combination of these two technologies enabled NIH researchers to identify over 100 proteins, which were altered during the benign to malignant transition in breast, ovarian, prostate, and esophageal cancer. These technologies also revealed the pathway that triggers cell death in cancer development.

The reviewers stressed the profound implications these technologies have on the diagnosis and treatment of cancer patients. Application of protein microarrays to patient biopsies can successfully monitor experimental therapies on the state of protein pathways that regulate growth and death of tumor cells. This, in effect, constitutes a direct approach to patient-tailored therapy.

The unveiling of the detailed, 3-dimensional structure of *proteasome* represented a major advance in X-ray crystallography. *Proteasome* is a large and complex protein–made up of 28 proteins of two types–responsible for protein degradation. Protein degradation is critical to cells because it serves to break down the building blocks, amino acids, for new protein synthesis or to remove excess or damaged proteins. From the detailed structure, scientists were able to infer the mechanism by which proteins fragment, the basis for generating antigens, the immune system's key defense against hostile invaders. This protein degradation pathway has broad implications for many severe immunological diseases–providing important drug targets for future treatments.

Imaging Tools and Applications

The application of Diffusion Tensor Magnetic Resonance Imaging (DT-MRI) to follow strokes in progress was a significant advance in imaging, according to most assessment members. DT-MRI is a sensitive technique that can measure the rate of water diffusion in the human brain. This rate of diffusion varies, depending on the direction and amount of fibers (brain white matter) associated with a tissue. The ability to measure varying rates along different directions makes DT-MRI unique and distinguishes it from other imaging techniques. This complex measurement can then be converted into an intricate three-dimensional color representation of tissues.

DT-MRI was successfully used to examine Wallerian degeneration, the permanent degeneration of nerve tissue often associated with chronic stroke. It accomplished this goal by identifying and differentiating white matter pathways that suffer from the lack of blood supply during strokes. Moreover, DT-MRI allowed scientists to perform detailed studies of the brain's structure, which previously could only be done with labor-intensive and invasive methods.

Animal Models

Transgenic technology represented another area of significant research advance this year. The ability to design animal models with specific and targeted genes allows scientists to understand complex diseases. A more "humanizing" mouse model–more closely resembling the human disease condition–was developed for Alzheimer's disease. TAPP (tau amyloid precursor protein), a double transgenic model from crossbreeding tau mutant mice with APP mutant mice, was the first model that established a connection between amyloid pathology and tangle formation. Tau (T) and amyloid precursor protein (APP) are two important proteins involved in the pathology of plaques, insoluble aggregates found in Alzheimer's patients' brains.

Animal models were also successfully developed to examine the role of estrogen in body fat accumulation with age. Several new transgenic mouse models were generated in which estrogen-related genes were eliminated. Both strains of mice, one lacking a form of the estrogen receptor and the other lacking the aromatase enzyme–involved in estrogen biosynthesis, resulted in an increase of fat tissue with age. These genetically modified mice provided powerful tools to study mechanisms by which estrogen influences age-dependent fat mass deposition. This type of study contributes significantly to the understanding of obesity, a growing public health concern in the U.S.

Another noteworthy animal model application was the development of yeast as a sensitive functional assay for rapid analysis of subtle changes in the p53 gene. Genetic mutation of p53 is found in the majority of human cancers and this type of functional analysis opens new possibilities for treatment strategies.

Gene/Cell Therapy

Gene or cell replacement continues to be a promising approach toward treating complex genetic disorders. A striking advance was the demonstration, for the first time, that endostatin could inhibit neovascularization (abnormal growth or proliferation of blood vessels) in the eye. Researchers successfully developed a technique, called viral vector transfer, to insert a gene sequence for endostatin in an animal model. Subsequent laser-induced neovascularization showed that high levels of endostatin could be sustained, thus prevented neovascularization. This proof-of-concept study represented a significant breakthrough for understanding vascular growth, the most common cause of blindness associated with eye diseases.

Another exciting advance related to the eye was the application of ribozyme therapy to retinal diseases. In this approach, researchers were able to deliver ribozymes–small RNA molecules–to the photoreceptor cells adjacent to the retina and effectively cured retinal degeneration up to eight months. This therapy was also proven to be effective when administered at a late stage of the disease. In ribozyme therapy, the inserted ribozymes serve to disrupt the gene expression of the mutated gene, while leaving the healthy one alone. This approach is particularly useful for dominantly-inherited diseases, where only one gene of the gene pair contains the mutated form responsible for the disease.

The isolation of pure epidermal (skin) stem cells from adult tissues received enthusiastic response from the reviewers as well. In this study, researchers were able to isolate stem cells from other types of skin cells–showing the capability of regenerating tissue and long-term gene activity. Until now, this had been a technical barrier for developing stem cells–a promising tool for bioengineering skin tissue– and ultimately, for treating skin diseases.

The delivery of growth factors to damaged tissues is a common method for stimulating tissue regeneration. NIH-supported researchers have developed a growth factor delivery system that responds to mechanical stress. The compressed polymer disks used in this device had a growth factor release rate up to five times the rate of the non-compressed disks.

These devices were also successfully implanted in control animals; those with implants exhibited enhanced blood vessel formation while those without implants showed no significant blood vessel formation. The increase in vascularization was also significantly higher in animals that received mechanical stimulation. This type of growth factor delivery system that responds to mechanical signaling has a wide range of applications, including regeneration and engineering of tissues, as well as general drug delivery uses.

Information Technologies

The reviewers highlighted three effective initiatives for disseminating health information to the general public. ClinicalTrials.gov provides patients, their families, and the public easy access to information about locations of clinical trials, their design and purpose, criteria for participation, and in many cases, further information about the disease and treatment under study. ClinicalTrials.gov currently contains information for almost 6,000 trials being conducted in almost 60,000 locations. The site generates more than two million hits each month, with over 5,000 unique users daily.

Profiles in Science (http://profiles.nlm.nih.gov/) is an archival collection of important papers, featuring some 20th century pioneers in biomedical research. This website represents a growing resource for students, educators, and researchers. The collections are particularly strong in the areas of cellular biology, genetics, and biochemistry, but also include related areas such as health and medical research policy, application of computers in medicine, and science education.

NIH is supporting an imaging archival network for storage, retrieval, and distribution of mammograms for clinical and research purposes. The network infrastructure is supported by *Next Generation Internet* (NGI) technologies, which ensures patient privacy and confidentiality with multilevel security embedded throughout the system. This provides an unparalleled opportunity to study and understand many epidemiological issues in breast cancer. In addition to access to screening data, it provides the opportunity to maintain and apply computer-aided diagnosis software at central, well-maintained computing resources to studies from all women.

Verification/Validation of Performance Measures and Data Issues

NIH's progress toward meeting this goal has been assessed by a working group of the Advisory Committee to the Director (ACD), NIH. The GPRA Assessment Working Group was composed of members of the ACD, the NIH's Council of Public Representatives (COPR), and selected members of the Institute and Center (IC) national advisory councils.

The assessment of NIH's research was based on data provided by the ICs (science advances, science capsules, and stories of discovery, as well as research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. Key references were provided for all science advances, science capsules, and stories of discovery. NIH also provided copies of full articles to the assessment working group whenever requested. (For a further discussion of this assessment process and the members of the Working Group, see Appendix 1).

The criteria that were developed and used to assess the outcomes of NIH research under goal b in FY 2001 are as follows:

The NIH biomedical research enterprise *has successfully met this goal* when its research yields new or improved instruments and technologies for use in research and medicine, and the instruments and technologies are published and/or disseminated or made available to appropriate populations.

The NIH biomedical research enterprise *has substantially exceeded this goal* when, in addition to fulfilling the criteria under *successfully met*, any of the following applies:

- Instruments and technologies improve quality of life. This includes new or improved ways to ameliorate/manage symptoms, relieve suffering, and restore/increase physical function/activity.

- Technical barriers are overcome so that investigations that were previously impossible are now possible.

- Instruments and technologies enable novel approaches to answering important biological and behavioral questions.

- Instruments and technologies are applicable to other disciplines, areas of research, or diseases.

- New/improved methods for generating, organizing, and disseminating genomic and other biological and behavioral information are developed.

The NIH biomedical research enterprise *has not met this goal* when its research fails to yield new findings related biological functions and behavior, or when new findings are not published and/or disseminated.

Goal c) Develop new or improved approaches for preventing or delaying the onset or progression of disease and disability.

Disease and disability exact enormous tolls on our society, both economic and personal. Rising health care costs highlight the importance of research that seeks to prevent disease and disability, or to delay and/or minimize its impact. Basic research is the first stage in the development of preventive measures. With a solid foundation of basic research, NIH-funded scientists have developed a broad range of preventive measures. These measures include interventions that change behaviors, screening tools that identify susceptible individuals, vaccines that block transmission of infectious diseases, and drugs that prevent the development of serious disease or disability in individuals who have already acquired a disease or who are genetically at risk.

Seemingly simple behavioral interventions can be very effective with respect to many types of diseases. For example, behavioral measures may be important in preventing the transmission of infectious diseases, in stopping or controlling alcohol and drug abuse or other abusive behavior, and in preventing obesity, diabetes, and cardiovascular disease. Behavioral measures such as the adoption of exercise programs or other changes in lifestyle can be very effective in preventing many diseases or impairments, and may eliminate the need for riskier or more expensive preventive measures, such as drug therapy.

In the best of both worlds, behavioral interventions, vaccines, and other interventions targeted at individuals with a genetic susceptibility would altogether prevent the development of disease or disability. However, it is inevitable that preventive measures aimed at limiting or controlling disease after its onset will be necessary. These may be microbicidal or physical measures that prevent the transmission of infectious disease, or drugs that reduce the transmission by lowering the concentration or viability when taken by individuals with low-level or pre-symptomatic indications of disease.

Targeting preventive and disease- or disability-delaying health interventions to at-risk individuals, as opposed to the general population, not only improves the effectiveness of these measures but also permits efficient use of health care dollars. To eliminate health disparities, targeting measures should include the identification of at-risk ethnic, gender, and socioeconomic groups, as well as identification of individual genetic susceptibilities. And studies that evaluate the relative effectiveness of expensive and inexpensive preventive measures contribute to the effectiveness of prevention efforts by enhancing their adoption by broad segments of the population.

For fiscal years 1999-2001, NIH measured its success under this goal against the broad target of progress in developing new or improved approaches for preventing or delaying the onset of diseases or disabilities. For fiscal years 2002 and 2003, NIH has put in place two representative subgoals to better define NIH's research plans under this goal. These subgoals focus on identifying modifiable risk actors for disease and disability and identifying, developing, and testing new or improved medications for the prevention of disease and disability. The importance of these subgoals is detailed below.

Subgoal c.1. Identify modifiable risk factors for disease/disability.

A first step in working towards the prevention of disease is the identification of modifiable risk factors. Such an assessment requires an understanding of the disease or disability, its physical characteristics, its cellular and molecular attributes, and the contributing genetic and environmental components. Basic research contributes fundamentally towards the goal of identifying risk factors, although until clinical results are seen, such contributions cannot be assessed. Thus, progress towards Goal C envelopes the background contribution of perhaps years of nonclinical research. By the very nature of research, this includes accrual of both positive and negative results, identification of contributing and noncontributing factors, and recognition of cellular features and molecular pathways both involved in and unrelated to disease progression. What emerges is the identification of primary risk factors that, when modified, can lead to substantial gains in overall health.

Just as the cessation of cigarette smoking can help to prevent lung cancer, many other behaviors that place an individual at risk for disease are modifiable. High blood pressure may be controllable by diet and/or medication, but unchecked, it increases the risk of stroke. Obesity is associated with coronary heart disease and diabetes. Unsafe sexual behavior and needle-sharing between intravenous drug abusers are risk factors for HIV infection and other sexually transmitted diseases; likewise, hepatitis virus transmission resulting from these behaviors places one at risk for liver disease, and the risk of liver failure is exacerbated if these individuals abuse alcohol. Less tangible but nevertheless modifiable factors are also known to affect the incidence of disease and disability. Compliance with vaccination guidelines can greatly reduce the contraction of many preventable diseases, but modification of factors as simple as hygiene and compliance with school policies on bringing sick children to school can aid greatly in lowering the spread of contagious diseases. Moreover, psychosocial involvement and increasing the level of physical and mental activity among the elderly can go far towards lowering the risk for dementia and physical ailments.

Research is needed to elucidate more precise risk factors so that modification can more effectively reduce the incidence diseases. More data are needed to prove or disprove the association of genes, environment, and behaviors with diseases, and because the incidence of some diseases remains high and has even increased in some cases, the identification of novel risk factors needs to be coupled with rigorous efforts at public education about the preventability or delay of diseases for which some modifiable risk factors are already known.

Subgoal c.2. Identify, develop, and test new/improved medications for the prevention of disease/disability.

The modification of key factors in disease progression relies not only on understanding the illness but also on the identification, development and ability to test medications that prove effective in delaying or preventing disease. The development of a single drug from pre-clinical research through FDA approval can take 10-15 years and several hundreds of millions of dollars of investment. On top of these daunting statistics is added a high rate of drug candidate failure with thousands of compounds needing to be screened before a few are selected for potential

benefit. These few candidates can then go through nearly the entire expensive course of development before only one is granted FDA approval, and even then, unforeseen toxicities can sometimes cause drugs to be withdrawn from the market. However, without these heroic measures being taken towards the development of medications for the treatment or prevention of disease, the human condition would undoubtedly suffer, and investments made in basic research would benefit little other than academic curiosity.

The government's role in the initiation, coordination, and propagation of the drug development process provides essential support and guidelines for investigators while ensuring as much as possible the safety of the public. The coalescence of experts in consortia strengthens this process, as do predictive bioinformatics tools designed for integrating the volume of information already accumulated with new insights as they develop. The call is made, therefore, to continue and, indeed, increase the efforts made thus far in the identification and testing of new drugs. Certainly, the development of medications for the prevention of diseases and disabilities will serve as useful milestones for assessing the fulfillment of this subgoal.

Annual Performance	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Progress in developing (or facilitating the private sector's development of) new or improved approaches for preventing or delaying the onset of diseases and disabilities -- and which reflect NIH responsiveness to emerging health needs, scientific opportunities, and new technologies.	★	★	◆		
c.1. Identify modifiable risk factors for disease/disability.					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇
c. 2. Identify, develop, and test new/improved medications for the prevention of disease/disability.					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇

★ Target Substantially Exceeded	◆ Target Successfully Met	◇ Target Active	✖ Target Not Met

Summary of Performance Results

- **The Assessment Working Group concluded that the goal was substantially exceeded.** The NIH Institutes and Centers submitted 127 scientific advances, science capsules, and stories of discovery (tabulated at the end of this section) that, in their judgment, demonstrated progress in developing new and improved approaches for preventing or delaying the onset of disease and disability. The Assessment Working Group concluded that the research outcomes submitted for FY 2001 not only addressed the goals of "Prevention" as outlined

(see Performance Assessment Approach above), but fulfilled the criteria for "substantially exceeding" this assessment area.

By its nature, preventive research is less dramatic than disease treatments or cures. It is the study of what does not occur. To demonstrate a lack of disease or delay in onset, studies in prevention often require long term, population-based projects. The Working Group felt strongly about emphasizing the incremental nature of these studies and recognizing that the successes of today culminated from work initiated years or even decades ago. Most importantly, the impact of preventive research on the overall health of the population is significant. Any assessment of the achievements of NIH-funded researchers must take into account that a sense of removal and/or abatement of health threats features prominently in the public's perception of research success made by the NIH.

The Working Group recognized that prevention requires physical intervention or behavioral change that can be enacted at the group level by public policy and/or individually by personal decision. Promoting change, however, requires the timely and effective dissemination of information. Specifically, educational programs should train clinicians to capitalize on "teachable moments" with their patients. Such opportunities relay information and provide reinforcement for behavior modification (which, in many ways, is the essence of prevention). Emphasis needs to be placed on the continued training of those in authority (policy makers) and those seen as knowledgeable (clinicians).

How the knowledge gained through NIH-funded research on prevention impacts the population needs to be assessed. Examination of the research outcomes for this year enabled the Working Group on Prevention to recognize studies resulting in substantial gains in prevention of disease and disability and also to identify studies that open doors to new areas of preventive research. In particular, an area needing research is behavior modification; this topic, along with environmental impact studies, will couple well with the results from the Human Genome Project. Eventually, individualized genetic susceptibility will be ascertained in the context of environmental and behavioral influences that affect gene expression and lead to disease.

In FY 2000, the Assessment Working Group concluded that NIH-funded research aimed at developing measures to prevent or delay the onset of disease and disability was noteworthy in many areas, including prevention of transmission of HIV and other infectious diseases; prevention of alcohol and drug abuse, and other abusive behaviors; prevention of Alzheimer's disease, obesity, diabetes, cardiovascular disease, and cancer; and prevention of diseases and disabilities acquired during pregnancy and childhood. NIH's phenomenal success in integrating basic science and behavioral efforts in the area of HIV prevention should be used as a model for other areas of research, such as research on drug addiction and violence.

In FY 1999, the Assessment Working Group acknowledged the importance of considering burden of illness in identifying especially noteworthy outcomes. They emphasized the importance of delaying the onset of disability and the tremendous implications this has for society in terms of health care costs and the toll on caregivers. The number of people that

might be affected by an intervention is equally significant, and simple interventions that have an impact on large populations are especially meaningful. The Working Group also highlighted a number of especially noteworthy outcomes that, in the judgment of the members, fulfilled the criteria for having substantially exceeded the goal. These advances fell into a number of broad categories: longitudinal studies; studies related to the prevention and treatment of mental illness across the life span; therapeutic interventions that also prevent or slow disease progression; behavioral interventions; and community-based interventions.

Research Outcomes and Their Significance

The Working Group noted that prevention, more than research in any other GPRA assessment area, delivers cost effective results. The trade-off is the length of time required for substantial benefits to be derived from preventive research. Public support is crucial to such endeavors, and the annual report on progress in preventive research should not undermine commitment to the short term, incremental advances. The group highlighted themes within preventive research studies in acknowledgment of the nature of this field.

The Working Group developed three major themes that encompassed the research outcomes they felt to be most significant from this past year. These themes encapsulated preventive research in the areas of: 1) behavior modification, 2) exposure to environmental factors, and 3) direct intervention. These topic areas focused the discussion while illustrating the interconnectivity of health defined through different avenues.

An underlying awareness throughout the discussion was of the tremendous insight provided to the field of prevention by the mapping of the human genome. Knowledge of gene susceptibilities will enable discrimination of genes versus environmental and behavioral effects that contribute to the development of disease. Moreover, understanding the genetic make-up paves the way to the engineering of highly individual prevention programs. However, regulation of gene expression as controlled by influences outside the body requires a great deal more research and, therefore, directs the future of preventive research.

Behavior Modification

The first theme recognizes behavior as a way to prevent disease and disability. In particular, exercise improves physical fitness, whether in women seeking to reduce coronary heart disease, older people with osteoporosis, female caregivers experiencing stress-induced high blood pressure and disrupted sleep, or children participating in a skeletal strengthening program of jumping. Children with Duchenne's Muscular Dystrophy do not benefit from exercise because of a faulty protein that cannot signal for increased blood flow to the muscle; however, prevention of disability could be improved with increased oxygenation of the muscles of these children during exercise. In a two-word summary, exercise works! Examination of exercise-induced health benefits, however, brings two issues to attention: 1) physical exercise alone may not provide all the benefits associated with an exercise routine, and 2) exercise requires behavioral modification.

Two studies delineated an important role of exercise by poignantly demonstrating how social engagement can provide health benefits that cannot be achieved by exercise alone. In one study, assisted walking for Alzheimer patients provided a chance for social interaction, and it was, indeed, the 30 minutes of conversation three times a week that reduced the patients' physical decline compared to the control group (no conversation during exercise). Likewise, a study of older people exercising in different environments led to the conclusion that a social setting improves the participant's psychological measures. The health benefits of exercise derive partially, if not fully, from addressing social needs for these two groups of people.

Two other studies bring to the forefront the necessity of modifying behavior in the interest of good health. One study showed that intensive lifestyle intervention was most effective in achieving exercise and weight control goals in overweight individuals at risk for type 2 diabetes. Medication alone had limited success and only in particular patient populations. This study indicated that behavior modification could be an effective means of lowering risk of disease. Unfortunately, differential responses to behavior modification may limit such successes: although both men and women in one study received physical activity counseling, only women derived any long term benefits. An understanding of what motivates people will greatly aid preventive research.

Other studies in preventive research focused on identifying ways to modify dangerous (that is, disease or disability inducing) behaviors in young people. Several studies assessed the effectiveness of intervention programs, focusing on decreasing such disparate occurrences as sexual activity, crime, high school drop out rates, or alcohol abuse. Each study revealed important factors that can positively influence behavior. A common theme in these studies was the importance of community—either as an arena for performing service-oriented activities or as a force for controlling behavior within the group.

Still other studies highlighted by the Working Group identified outside influences or personality variables that affect dangerous behaviors. Promotions by cigarette companies exemplify an outside influence that increased smoking in adolescents. Rebelliousness and risk taking behaviors in 5th graders predicted cigarette smoking by 12th grade. And early onset drinkers took more risks, which identified this group as likely to sustain more injuries. Only one study noted a positive correlation between a predictive element and prevention of dangerous activities: that of virginity pledges by some adolescents. The Working Group applauded these research outcomes because each identified behavior or outside influence could potentially be manipulated to decrease disease and/or disability.

Exposure to Environmental Factors

The second theme could encompass many more studies than those highlighted by the Working Group; the desire to understand physiologic reactions to man-made influences in our environment stimulates many research projects. These types of studies impact nation-wide behavior by providing a basis for public policy that protects health. Several scientific outcomes discussed by the Working Group influenced the health of the next generation. For example, maternal exposure to polybrominated biphenyls (PBB) altered normal pubertal development in

girls, whereas maternal exposure to a metabolite of the chemical DDT increased the incidence of both premature births and unusually small babies. Premature birth is a major risk factor for infant mortality. Similarly, a scientific outcome mentioned by the Working Group attributed ultraviolet-□ radiation to inability of an amphibian to reproduce.

The Working Group highlighted several other scientific outcomes because these studies clearly linked the impact of human activity on the environment with consequences to human health. Modest increases in ambient ozone concentration are associated with increases in respiratory illnesses in school-aged children. Nitrate levels in drinking water increase a woman's risk for bladder and ovarian cancer. Exposure to small particles in the air–from combustion processes in car engines, power plants, refineries, smelters, and other industries–appears to increase the risk of cardiovascular disease. These reports seem straightforward, but the study of the effect of nitrates in the drinking water also revealed a decreased incidence of uterine and rectal cancer in women. These studies point to the complex nature of environmental pollutant exposure and the need to understand its mechanism.

A complicating factor in linking disease with environmental triggers is that of combined or multiple environmental exposures. Parkinson's disease may be the result of multiple insults, such as with the herbicide, paraquat, and the fungicide, maneb, or of continuous exposure to the organic pesticide, rotenone. Again, environmental agents cannot be condemned or repudiated without exhaustive research into their mechanism of action. In this regard, the Human Genome Project has the potential to have tremendous impact on the understanding of the interaction of gene susceptibility and environmental influences. Ultimately, prevention in the area of environmental threats requires the enacting of sound public policy based on robust scientific understanding. Policy makers were especially urged to note the results of the study linking air pollution and heart attack risk; this was considered one of the most tangible research efforts linking combustion-generated pollution to an almost immediate impact on the population.

Direct Intervention

The third theme, direct intervention, derived from recognition that subgroups of highlighted science advances focused on a particular disease or type of injury or, in the case of vaccines or estrogen, were a particular way to induce prevention. The diversity of the studies brought up in discussion impressed the reviewers, and, as a group, the Prevention assessment members condoned emphasizing in the GPRA report first one subtheme then another. Finally, each person had contributed at least one new subtopic to the discussion. Eight dominant topics emerged and will be detailed below. They include: estrogen, osteoporosis, diabetes, the brain, mental health, vaccines, stroke, and Alzheimer's disease. One unique research outcome did not fit in any subtheme, but was applauded for its counter-intuitive finding that high levels of cat allergen decrease risk of sensitization to other allergens.

Discussion was not limited to the science advances, and, in particular, three stories of discovery provided the Working Group with insight into problems and strengths of preventive research. The awareness that HIV can be transmitted through breast milk clearly needs to increase in countries with high rates of both HIV infection and breastfeeding, but this knowledge many not translate directly into prevention of disease or disability. Often times, mothers of resource-poor

countries do not have the choice not to breastfeed. Unfortunately, HIV-infected mothers are three times more likely to die if they breastfeed rather than bottle feed their infants, and infants whose mothers die are eight times more likely to die than infants whose mothers survive, even taking their HIV infection status into account.

Obviously, the "breast is best" campaign needs to be tempered in the face of other conditions such as HIV status and poverty. Seemingly conflicting messages sometimes arise from preventive research and the Working Group recognized the difficulty in disseminating such information to underdeveloped countries. No solution to these problems could be envisioned except to increase efforts to prevent HIV with a vaccine.

A second story of discovery detailed studies on post-traumatic stress disorder (PTSD). The Working Group felt that this line of research deserved accolades and heightened awareness of the interrelationship between mental health research and other prevention studies. It was acknowledged that individuals with PTSD are not likely to engage in the kinds of behaviors that will prevent other diseases, such as type 2 diabetes. The environmental/behavioral side of the "nature vs. nurture" equation involves several layers of complexity and connectivity. By upsetting the "nurture" part, PTSD can be indicative of other poor health outcomes.

A third story of discovery also led to a discussion about how research in one area impacts another. The original discovery that calorie restriction increases life span now influences thinking about how diabetes and heart disease is prevented through diet and how the cell responds to stress, particularly oxidative stress. The theme that preventive research progresses by incremental advances in disparate areas reoccurred in the Working Group discussion as members recognized the importance of reporting on advances in one area to aid advancement in other areas.

The following paragraphs explore the subthemes within the direct intervention theme. The individual studies of the science advances that were highlighted often fit two different subthemes; consequently, an impressive research outcome could be lauded from several perspectives. An example of this is the study of vaccination in an animal model of Alzheimer's disease: the tremendous advances in understanding Alzheimer's disease can be illustrated by an ability to prevent disease in a mouse model (subtheme: Alzheimer's disease) and one of the finest examples of preventive research is a successful vaccine, as was engineered in a mouse model of Alzheimer's disease (subtheme: vaccines). The eight subtopics again demonstrate the complex and long-term nature of advances in preventive research and, while not always adding ways to prevent disease or injury, they add to knowledge that will hopefully result in preventive measures.

Estrogen. Two research outcomes illustrated the health benefits of receiving estrogen replacement therapy (ERT). A reduction of systolic blood pressure occurs in postmenopausal women receiving ERT and the risk of cataracts decreases with long-term ERT. On the other hand, not all estrogen therapy is protective. A striking outcome linking plant estrogens with animal cancers dispels the assertion that soy—often an important part of a "natural and healthy" diet—is indeed healthy.

Other aspects of what the Working Group members called the estrogen story include the recognition that a synthetic form of estrogen, DES, increases breast cancer risk and that a metabolite of the pesticide DDT, used to kill malaria-transmitting mosquitoes, increases premature births—a major risk factor for infant mortality. Insight into acceptable levels of therapeutic estrogen came from research on osteoporosis where lower doses of estrogen protect against low bone mass as effectively as higher doses, but with fewer side effects and potentially less risk of uterine and breast tumors.

Osteoporosis. As demonstrated by one highlighted research outcome, a direct intervention to decrease bone loss in an elderly population involves increasing dietary protein. Likewise, osteoporosis can be reduced in women by giving estrogen, preferably, as noted above, in a lower, rather than higher, dose. These two studies on osteoporosis commanded the attention of the Working Group because they contribute to a bigger story and, therefore, are important as incremental steps. Moreover, the first study exemplifies the population-based research needed for advances in preventive research.

Diabetes. The magnitude of the type 2 diabetes problem in the United States and the associated obesity problem astonished Working Group members. Their psychological balance was the science advance that epitomized preventive research in its use of long-term, population-based data. The 20-year study using a cohort of 121,000 female nurses convincingly showed an increased risk of heart disease in diabetics, thus calling attention to a need to develop appropriate prevention and therapeutic strategies. In addition, the study demonstrated that this risk could be markedly reduced with exercise. On the basis of this and other reports, national diabetes associations now recommend aggressive management of diabetic patients to reduce cholesterol, high blood pressure, smoking, and obesity. Exercise and diet play important roles in diabetes management and cardiovascular disease prevention.

A second highlighted study creatively questioned whether breastfeeding reduces the risk of teenage obesity. Not only did results show that infants who were fed breast milk more than infant formula decreased their risk of being overweight, but the study showed that longer duration of breastfeeding correlates with less of an overweight problem in adolescence. Promotion of breastfeeding may help abate the rising prevalence of obesity in the United States and in other developed countries.

The Brain. Several research outcomes describing prevention of brain injury appealed to the Working Group members because of these studies' applicability to other research or because they opened doors to previously unexplored areas of research. For example, the drug allopurinol appears to play a neuroprotective role in infants with high-risk of heart defects, and creatine can be used as a dietary supplement to protect neurons from damage caused by temporary energy deficiencies. Both studies also impact prevention of neurological damage in such disparate situations as stroke and trauma, or in patients with Parkinson's or Huntington's disease.

On the other hand, dietary restriction plays a role not in protection but in production of nerve cells and also increases growth factors in the brain. These findings stimulate further research into ways to combat age-related neurodegenerative disorders. Likewise, another study opens new research into brain plasticity: language appears to be acquired in a crucial learning period,

through a complex interaction of biology and culture. Such findings translate into prevention of language problems through understanding the windows of opportunity for education.

Mental Health. Although specific science advances were not highlighted, the Working Group members cited as significant the innovative research investigating mental health problems and biological disease. Two appropriate studies are summarized as examples. In the first study, an increase in social ties and in activities, particularly intellectual, was predictive of better cognitive function and was associated with a decreased risk of Alzheimer's disease.

The second study demonstrated for the first time a biological effect of stress on the skin's barrier function. Furthermore, a scientific capsule about the effectiveness of depression intervention in college-age women achieved recognition by the Working Group members because it typifies a primary preventive approach and has the potential for significant success. The interface between mental health problems and biological disease incites a relatively new arena for preventive research.

Vaccines. Vaccines epitomize an effective outcome of preventive research. Although considered traditional in approach, vaccines themselves have been modernized. Both recombinant DNA technology and naked DNA are now used to generate new vaccines. The fact that vaccines have a 'corner of the market' in preventive research is evidenced by the numerous science advances and science capsules selected by NIH institutes and centers for review by GPRA evaluators. Diseases for which vaccines are being produced include otitis media (ear infection), Ebola, dengue virus, AIDS, and Leishmania (parasite). A more effective tuberculosis vaccine is also under development.

The one vaccine study evoking the most attention by Preventive Working Group members not only prevented memory impairment, but also resulted in better learning and memory performances by transgenic mice modeling Alzheimer's disease. These mice had been injected with a fragment of the amyloid precursor peptide called amyloid-beta, and, in the long-term study, these mice had partial reduction of amyloid deposition. No difference was observed in amyloid pathology in mice vaccinated in the short-term, but these mice demonstrated an increase in microgial activation. The results of this and the other studies propel further vaccine research.

Stroke. A science capsule confirms that eating fish two to four times a week reduces the risk of hemorrhagic stroke in women by approximately one-half. This study was noted because of its relationship to preventive studies on behavior modification and on the connection between obesity and diabetes. Working Group members also recognized its cost effectiveness.

Usually, individual science advances shaped the reviewer's impressions of the field's forward momentum. However, the story of discovery entitled "Preventing Strokes" embodied several of the features that members of the Working Group wanted to highlight about preventive research. These research features include: a multifaceted approach; a long-term nature; incremental results; collaborative and multidisciplinary sponsorship; disease assessment across gender, ethnic, and age boundaries; an emphasis on dissemination of results, and most importantly, significant overall impact on health.

The research on strokes requires a multifaceted approach because millions of Americans live with a variety of risk factors. The gains in stroke research were acquired incrementally, but over a 46-year period, the age-standardized stroke death rate declined by 70 percent for the U.S. population. A variety of studies by a variety of research groups have contributed to the knowledge base and to the bridging of gaps in research. Finally, clinicians and the public are continually being educated about important research findings through specific education programs and a website maintained by NIH. Future directions on stroke research will explore genetic tests, tailored preventive measures for each individual, the possibility of vaccination, and the link of stroke to infections or inflammation within blood vessels.

Alzheimer's Disease. A final subtheme of direct intervention centered on prevention of Alzheimer's disease and the disability associated with this disease. Earlier discussions of other themes in preventive research touched on the science advances that could also be mentioned here: the significance of improving mobility in nursing home residents with Alzheimer's disease to counteract functional decline; the importance of physical, intellectual, and social stimulation in protecting against cognitive decline in, and risk of, Alzheimer's disease in the elderly; and the enthusiasm generated by development of a vaccine that prevents age-related memory deficits in a transgenic animal model of Alzheimer's disease.

These studies illustrate that progress in preventive research cannot be fully appreciated by classification under one or two broad themes. Two other studies on Alzheimer's disease represent tremendous potential for both the immediate and the more distant future. Statins, the most common form of cholesterol-lowering drugs, reduce the risk of dementia in patients with high cholesterol and decrease the mean number of amyloid deposits in the brains of mice modeling Alzheimer's disease.

Another study highlighted by the reviewers identified the enzyme responsible for generating the peptides that became deposited as plaque in the brains of Alzheimer's patients. This finding makes possible research to inhibit amyloid plaque development and, hopefully, Alzheimer's disease itself. The preventive potential generated by this science advancement is undeniable and helped convince the Prevention Working Group that advances generated by the NIH in the field of prevention justify a rating of "substantially exceeding the goal" in this area of research endeavor.

Verification/Validation of Performance Measures and Data Issues

NIH's progress toward meeting this goal has been assessed by a working group of the Advisory Committee to the Director (ACD), NIH. The GPRA Assessment Working Group was composed of members of the ACD, the NIH's Council of Public Representatives (COPR), and selected members of the Institute and Center (IC) national advisory councils.

The assessment of NIH's research was based on data provided by the ICs (science advances, science capsules, and stories of discovery, as well as research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. Key references were provided for all science advances, science capsules, and stories of discovery.

NIH also provided copies of full articles to the assessment working group whenever requested. (For a further discussion of this assessment process and the members of the Working Group, see Appendix 1).

The criteria that were developed and used to assess the outcomes of NIH research under goal c in FY 2001 are as follows:

The NIH biomedical research enterprise *has successfully met this goal* when its research yields new or improved approaches for preventing or delaying the onset or progression of disease and disability.

The NIH biomedical research enterprise *has substantially exceeded this goal* when, in addition to fulfilling the criteria under *successfully met*, any of the following applies:

- Findings demonstrate potential to lead/contribute to the development of preventive measures or strategies for delaying the onset/progression of disease and disability.

- Research-based advances and public health campaigns result in broad health impacts–such as reductions in morbidity and mortality, changes in health-related behavior, amelioration of health disparities.

- Prevention strategies are applicable to other disciplines, areas of research, or diseases and conditions.

- Discoveries improve quality of life by preventing or delaying the onset/progression of symptoms, suffering, loss of function, and/or injury.

The NIH biomedical research enterprise *has not met this goal* when its research fails to yield new findings related biological functions and behavior, or when new findings are not published and/or disseminated.

The Working Group operated and conducted its assessment in an independent manner. The data on research accomplishments considered in the course of the assessment will be available to the public.

Goal d) Develop new or improved methods for diagnosing disease and disability.

Disease diagnosis is a practical area that links the growing body of basic biomedical knowledge to the health care system and the health care consumer. An understanding of genetics and the molecular basis of disease are particularly applicable to improvements in diagnosis and development of new diagnostic tests. Frequently, basic molecular research identifies a molecule or metabolic byproduct that has tremendous value in diagnosis. In addition, other areas of technological innovation provide information for diagnosis, and practical application of research in imaging and spectroscopy is a potential source of valuable new instrumentation.

Early and accurate diagnosis of disease often has an impact on treatment. There are many cancers for which early diagnosis may be the key to survival. For some conditions, disability can be controlled or limited if treatment begins early. Possible features of an advance in diagnosis include increased accuracy, the replacement of an invasive technique with an approach that is non-invasive, and the ability to identify a condition that puts a patient at risk before disease symptoms are apparent.

For fiscal years 1999-2001, NIH measured its success under this goal against the broad target of progress in developing new or improved diagnostic methods that are more accurate, less invasive, and/or more cost effective. For fiscal years 2002 and 2003, NIH has combined this goal with goal e, developing new or improved methods for treating disease and disability. The new goal will be, develop new or improved methods for diagnosing and treating disease and disability. As with the previous research outcomes goals, NIH has put in place two representative subgoals to better define NIH's research plans under this new, combined goal. These subgoals focus on developing and applying powerful new imaging, genetic, and biological technologies to enable early and more precise diagnosis and intervention, and on identifying and applying knowledge about various factors, including gender, race, ethnicity, and socioeconomic status, to improve diagnostic reliability and treatment response. The importance of these subgoals is detailed below.

Subgoal d.1. Develop and apply powerful new imaging, genetic, and biological technologies to enable early and more precise diagnosis and intervention.

The diagnosis of disease requires the art of a physician and the science of a researcher. In the past, physicians looked for the recurrence of symptoms as a sign that a treatment for leukemia or lymphoma had not succeeded. By the time a relapse had occurred, however, it was often too late to save a patient. Presently, minimal residual disease following treatment in cancer patients is diagnosed at the single cell level, and more aggressive retreatment holds the promise of higher remission rates. The diagnosis of minimal residual disease could not be made without applying the latest detection technologies developed by researchers in the laboratory. Likewise for breast cancer, early diagnosis is aided by early detection. Coupling an early self-detection with the powerful imaging technology developed in recent years for mammography has greatly aided in

the earlier diagnosis of breast cancer and undoubtedly resulted in the survival of more breast cancer patients.

New technologies are needed not only for cancer diagnosis but for myriad other diseases. Diabetes and its associated disabilities of the feet, eyes, and kidneys might be delayed or even prevented if controlled earlier in the progression of the disease. The suffering of lupus patients might be controllable years earlier than usual if a proper diagnosis were made; yet a single, unambiguous diagnostic marker for lupus does not exist, and a panel of markers as well as a patient's disease history must necessarily be evaluated before a lupus diagnosis can currently be made. The challenge is to develop assays of higher sensitivity and specificity, and more powerful imaging technologies are needed to increase our ability to detect disease. Our ability to create better biotechnology holds the promise of enabling earlier and more precise diagnosis of disease and earlier and more directed intervention for disease prevention and treatment.

Subgoal d.2. Identify and apply knowledge about factors, including gender, race, ethnicity, and socioeconomic status, to improve diagnostic reliability and treatment response.

Drug safety and efficacy studies are initially conducted in highly controlled experiments using inbred animals of the same sex and age. However, researchers understand that a drug safely tolerated in three-month old male mice of similar genetic origin (race) does not mean that the same drug will be uniformly tolerated by all members of a racially diverse human population, or even within the same race by people of different ages or genders. It is now well established that there are genetic factors responsible for diminishing or enhancing the efficacy of drugs, and these factors often differ between races, ages, and genders. Factors other than those contributed by genetics can also influence how well drugs are tolerated as well as their efficacy in individual patients. Such factors can be related to socioeconomic status, including alcohol consumption and dietary habits, or across socioeconomic differences, as in the case of the influence of multiple medications taken simultaneously (polypharmacy).

Whether the intent is to improve diagnostic reliability or the response to treatment, it is important to be cognizant of factors that can have an impact on those outcomes. Although the science of individualized medicine is in its infancy, it can only evolve if researchers are diligent about relating the identification of diagnostic markers or drug efficacy findings to the demographics of the groups being assessed. Only then will conflicting findings between different researchers studying the same drug be able to be resolved, and only then will the variable toxicities observed within a single clinical trial be understood. With this discernment, clinicians will be able to prescribe different doses, different regimens, and perhaps entirely different medications for the same disease among different patients, and a much higher efficacy should be able to be achieved with a much lower level of toxicity. Importantly, these improvements will be based on known and yet to be identified differences in factors that exist between people of different age, race, gender, and socioeconomic status.

Annual Performance	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Progress in developing (or facilitating the private sector's development of) new or improved diagnostic methods that are more accurate, less invasive, and/or more cost-effective -- and which reflect NIH responsiveness to emerging health needs, scientific opportunities, and new technologies.	★	★	★		
d.1. Develop and apply powerful new imaging, genetic, and biological technologies to enable early and more precise diagnosis and intervention.					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇
d.2. Identify and apply knowledge about factors, including gender, race, ethnicity, and socioeconomic status, to improve diagnostic reliability and treatment response.					
Annual milestones which may include descriptions of science advances and stories of discovery; and initiatives such as Requests for Announcements (RFAs), Program Announcements (PAs), conferences and workshops.				◇	◇

★ Target Substantially Exceeded	◆ Target Successfully Met	◇ Target Active	✖ Target Not Met

Summary of Performance Results

- **Important new diagnostic methods that use a range of approaches, including imaging and spectroscopy, molecular analysis of body fluids, genetic analysis of tumor tissue, and cell biology techniques, recently have been made available or are in development.** The NIH's institutes and centers submitted 69 science advances, science capsules, and stories of discovery (tabulated at the end of this section) under goal d for FY 2001. In the judgment of the assessment working group, the NIH has "substantially" exceeded its target in developing new or improved instruments and technologies for use in research and medicine (see *Performance Assessment Approach* criteria above for "substantially exceeding" goal).

  In FY 2000, NIH's Institutes and Centers submitted an array of scientific advances, scientific capsules, and stories of discovery drawn from many different areas of biomedical research that, in their judgment, demonstrated progress in the development of new or improved methods for diagnosing disease and disability. Some studies described new diagnostic assays that open possibilities for better detection or more accurate predictions. The identification of genetic markers in many studies can impact other diseases and even other areas of research, as mechanisms of disease unfold from the genetic information. Several studies capitalized on technology to develop less invasive and painful methods of diagnosis. The Assessment Working Group especially emphasized evidence of the innovative use of current tools.

  In FY 1999, the Assessment Working Group concluded that the outcomes demonstrated that NIH had significantly contributed to the development of new or improved methods for diagnosing disease. The research outcomes demonstrate new or improved diagnostic methodologies that are more accurate, less invasive, and/or more cost-effective, and are

responsive to emerging health needs, scientific opportunities, and new technologies. The new or improved diagnostics that have or will arise from this research will ultimately improve human health and quality of life. For example, earlier and/or more accurate diagnosis can lead to earlier and more informed treatment decisions, and this may contribute to more positive health outcomes. In their discussion, members of the Working Group identified a number of important themes or categories of research outcomes related to diagnosis, discussed the significance of these types of findings, and highlighted a number of research outcomes that they judged to be especially noteworthy.

Research Outcomes and Their Significance

The Working Group enthusiastically discussed a number of important advances related to diagnosis, including some that are ready for immediate application. Many advances are based on genetic and molecular analysis of genomic data. There are promising new spectroscopic approaches, as well. New, non-invasive tests for various cancers and other conditions are in development. In addition, investigators report a useful new tool to replace the endoscope for diagnosis of Barrett's esophagus and other pre-cancerous conditions.

Tools for Immediate Application

New device to diagnose Barrett's esophagus and other pre-cancerous conditions. Barrett's esophagus, a condition that develops in some people who suffer from chronic heartburn, frequently develops into a type of cancer known as adenocarcinoma. The prognosis for patients diagnosed with adenocarcinoma is poor, but if the condition is identified early (at the stage where it is called Barrett's esophagus), the chance of successful treatment improves significantly. To examine the esophagi of patients with chronic heartburn and determine if they have Barrett's esophagus, physicians rely on painful and repetitive endoscopic examinations and frequent biopsies. Both techniques must randomly hit the right spot in the esophagus to detect Barrett's esophagus.

A promising new device combines three optical techniques, fluorescence, reflectance, and light scattering, to provide reliable diagnosis of the condition. The device is highly sensitive and less intrusive than random biopsies. It allows physicians to monitor patients with chronic heartburn more easily and look for signs of Barrett's esophagus. Although the device was tested on the esophagus, it can also be used to examine pre-cancerous tissue in the oral cavity, cervix, lungs, breasts, and the gastrointestinal tract.

Detection of bladder cancer in urine. Researchers have developed a urine test that detects survivin, a protein found in bladder cancer cells. The simple, non-invasive test uses an antibody to detect survivin in urine. Results indicate that sensitivity of the urine survivin test for new or recurrent bladder cancer was 100%. The test appears to be superior to existing tests for bladder cancer in terms of sensitivity, specificity, ease of use, and cost effectiveness.

Molecular screening for hemochromatosis. Hemochromatosis is a treatable disorder involving deposition of iron in tissues, especially liver and joints. People who have the disease have

mutations in both copies of the hemochromatosis gene (HFE). Researchers used molecular techniques to screen relatives of people with the disease and identify family members who also have two copies of the mutated HFE. This screen allows early detection–prior to disease onset– and appropriate treatment for relatives of affected individuals.
Diagnostics by Genetic Markers

Improved diagnosis of oligodendroglioma. More than 100 types of brain tumors are recognized by conventional pathological criteria. Malignant gliomas are the most common among these. A particular subtype of glioma, oligodendroglioma, is more likely than most to respond to drug therapy. The first step in diagnosis is distinguishing subtypes of oligodendrogliomas from each other. Recently, scientists identified genetic markers that can be used to discriminate among tumor types and identify subtypes of oligodendrogliomas. This information is useful in predicting response to chemotherapy. By performing genetic analysis of cells derived from the tumors, scientists can divide the tumors into four subgroups, depending on whether they had lost pieces of chromosomes 1 and 19 (called 1p and 19q) and whether there is a mutation in the TP53 gene.

The study found that tumors with loss of both 1p and 19q had a strong response to chemotherapy and long survival; other tumors with alterations in 1p also responded to drug therapy, but not as well; tumors with mutations in TP53 responded to chemotherapy but the tumors recurred quickly; tumors with no loss of 1p and no mutations in TP53 responded poorly to chemotherapy. This study provides information that might prove to be extremely valuable to clinicians in determining the best course of treatment for a patient with a subtype of malignant glioma. The Working Group pointed out that oligodendroglioma is a relatively common type of cancer, which means that the improvement in diagnosis will have substantial impact on health care choices.

Non-invasive test to detect kidney transplant rejection. Rejection of a transplanted kidney is not uncommon. About 35% of organ recipients have an acute (sudden and severe) episode of rejection within the first year after transplantation. Therefore, frequent monitoring is required. The current method for monitoring rejection is insertion of a long needle into the kidney through an incision in the skin and removal of a small sample of tissue for examination under the microscope (needle biopsy). In addition to being invasive and painful, needle biopsy can lead to complications, including kidney failure.

Scientists are in the process of refining a non-invasive approach to monitoring kidney rejection. The test measures levels of specific RNA molecules in the urine. The RNAs to be measured are characteristic of cells that would attack the organ. The test should allow doctors to predict rejection and begin treatment before the transplanted kidney is severely damaged.

A saliva test for diagnosis and management of AIDS. NIH-supported investigators have developed technology to rapidly identify variants of the HIV virus in saliva. The test can differentiate between the R5 and X4 variants of the virus. The R5 variant usually predominates early in the course of infection, while the X4 variant appears later. It is reasonable that physicians might alter therapy based on monitoring a patient's virus and knowing the stage of viral evolution.

Detection of colorectal cancer in stool sample. Colorectal cancer is the second largest cause of cancer death in the U.S. Diagnostic tests for colorectal cancer include examination of stool for blood, a method that detects only a fraction of cases, and colonoscopy, which is considered invasive. Scientists are in the process of developing a genetic test to be used on stool. Almost all of the DNA in stool comes from intestinal tract bacteria, and it is a daunting task to find, identify, and characterize the small fraction containing tumor DNA, if it is present. Investigators have developed a reliable method for purification and amplification of tumor DNA from stool and have made significant progress in analyzing the tumor genes TP53, BAT26, and K-RAS. When available, the test will be an extremely useful diagnostic tool.

Progress in developing a blood test to detect ovarian cancer. If detected early, the five-year survival rate for ovarian cancer is 93%. However, the disease has few symptoms in the early stages and less than a quarter of ovarian cancers are detected early. At present, only 46% of women diagnosed with ovarian cancer will survive five years or longer. Scientists are working to develop a non-invasive test that could be performed routinely to improve early detection of the disease. They identified five likely ovarian cancer genes for the test and have developed methods to measure the products of two of them, mesothelin and HE4, in blood. When the blood test is developed further it may be used to indicate which women should receive the more expensive test, transvaginal sonography.

Genetic diagnosis of cancer risk. Investigators have developed an approach to diagnosis based on creation of cell lines that contain components of mouse and human cells. The new diagnostic tool, called "conversion," is a variation of a laboratory technique that had been used for other purposes for a number of years. Recently, researchers simplified the approach and used the technique as a means of identifying genes for colorectal cancer that might not be seen using conventional genetic tests. The gene conversion approach is also applicable to other hereditary cancers, including breast and kidney cancer, as well as a wide variety of neurological and cardiovascular diseases.

Identification of the most aggressive cancers. Genomic instability is a hallmark of the most aggressive cancers. A number of cancers, including breast, colon, and lung cancer, exhibit genomic instability. Researchers found that the expression of the MAD2 protein is linked directly to genomic instability. Monitoring MAD2 levels may make it possible to more accurately predict a tumor's aggressiveness.

Hormone replacement therapy and heart attack risk. Hormone replacement therapy (HRT) appeared to increase the risk of heart attack for some women. A recent study indicated that the women on HRT who had both high blood pressure and a mutation in the gene for prothrombin (an enzyme that regulates blood clotting) were at significantly greater risk for cardiac arrest than hypertensive women on HRT who did not have the prothrombin mutation. If these results are confirmed, post-menopausal women eventually may be screened for prothrombin mutations when they and their doctors decide whether to use HRT. That way, doctors can identify a subset of women who should not use HRT because they are at risk for heart attack.

Lumbar disc disease. Lumbar disc disease (LDD) is a common cause of low back pain that frequently presents as a disc rupture or herniation with possible pain in buttock, knee, calf, or

foot. Activities, behaviors, and characteristics that appear to contribute to LDD include heavy lifting, twisting, vibration, smoking, taller height, and obesity. There also appears to be a genetic component. Recent studies identified a variant of collagen IX (a connective tissue protein) as a risk factor for LDD. Individuals who have the variant gene appear to have three times the risk of developing LDD than those who do not have the variant gene.

DNA sequence of Escherichia coli O157:H7. Serious illness caused by the food-borne pathogen Escherichia coli (E. coli) O157:H7 has increased since it was first observed in 1982. The pathogen is currently considered a public health problem. Recently, investigators obtained the DNA sequence of the infectious organism and compared it to the benign form of E. coli that was sequenced in 1996. Some important and surprising differences were noted between the two strains.

E. coli O157:H7 has a much larger genome and contains approximately 1,300 genes not found in the harmless strain, including some genes that are very similar to those of the bacterium Salmonella and the plague-causing organism Yersinia. E. coli O157:H7 also has a gene that encodes the extremely potent Shiga toxin, originally found in the dysentery-causing microorganism Shigella. Since infection with Shigella is managed differently than infection with E. coli O157:H7, it is important to be able to differentiate between the two organisms. An eventual test to differentiate between the two organisms may stem in part from the DNA sequence. In addition, having the sequence in hand is a preliminary step toward developing an effective vaccine against or treatment for the infection.

Single nucleotide polymorphisms and haplotypes: diagnostic tools stemming from the human genome sequence. Human beings are 99.9% identical in their genetic makeup. The 0.1% that is different includes the genetic variation that leads to differences in risk of disease. Places where the DNA sequence varies between individuals by a single nucleotide are called single nucleotide polymorphisms, or SNPs. The Human Genome Project and the private sector are working to identify SNPs and make the information available to researchers without intellectual property restrictions. So far, nearly 3 million SNPs have been identified and entered into public databases. Haplotypes are closely linked genetic markers, including SNPs, that are present on one chromosome and which tend to be inherited together. The Human Genome Project is in the planning stages of developing a haplotype map of the human genome. The Working Group discussed the fact that when more data are available, SNPs and haplotypes will be powerful tools for diagnosis of common disease. The groundwork for future advances is being laid now.

Spectroscopy and Imaging

***Images of Alzheimer's disease pathology in the living brain*.** Alzheimer's disease cannot be diagnosed with certainty until after the patient has died. In the post-mortem brain of a person with Alzheimer's disease there are two defining features of the disease, amyloid plaques and neruofibrillary tangles. Scientists who are working on a mouse study are making progress in obtaining images of the living brain. As part of a study to find methods to clear plaques from brain, transgenic mice are being used to test new imaging techniques on brains of living animals.

Scientists have been able to image the mouse brains with multiphoton microscopy, which provides 100 times greater resolution than other in vivo imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Multiphoton microscopy has allowed the investigators to view very small brain lesions (such as plaques in living mice) as part of an immunotherapy experiment. The approach is still in the experimental stages.

A new method of functional MRI (fMRI) is being developed that is sensitive to resting brain function. Studies are being done in humans and transgenic mice. Using fMRI, investigators generated brain maps that highlighted structural and functional architecture of the hippocampus. This precise method of mapping could eventually be used to identify persons with loss of neurons in very specific brain regions, for example, in preclinical identification of individuals at risk for Alzheimer's disease.

A role for mass spectrometry in proteomics. The Working Group discussed the continuing importance of mass spectrometry (MS) as an analytical and diagnostic tool. MS, first developed almost one hundred years ago, is used to measure and characterize particles that are far too small to be observed visually or weighed on a conventional scale. NIH has supported decades of progress in MS technology. Early uses for MS included analyzing simple organic mixtures (for example, petroleum).

In the 1960s, NIH-supported scientists, notably Dr. Klaus Biemann at the Massachusetts Institute of Technology, combined MS with gas chromatography (GC/MS) to analyze blood and urine of patients suspected of having metabolic disorders. By the 1970s, the usefulness of MS in analysis of body fluids was apparent, and commercial laboratories began to offer GC/MS services to hospitals nationwide. In the 1980s MS technology improved to the point where more fragile compounds could be studied. This type of MS is called matrix-assisted laser desorption ionization (MALDI) and electrospray ionization (ESI).

MALDI and ESI can be used to analyze extremely small samples of very fragile protein molecules. MS was used to determine the three-dimensional structure of the prion protein, which is responsible for mad cow disease and other human neurological disorders. MS provided information on how proteins on the surface of the AIDS virus allow it to evade the human immune system. MS is also used to study proteins on tumor cells.

Today's state-of-the-art MS devices are being used in the emerging field of proteomics. The goal of proteomics is to detect, evaluate, and understand the thousands of proteins encoded by the human genome. Scientists are using integrated technologies that include MS to obtain and analyze data at remarkably high rates (in some cases more than 100 acquisitions per second). The Working Group emphasized that proteomics is likely to provide major advances relevant to the diagnosis of disease and that MS will be fundamental to the proteomics field.

Verification/Validation of Performance Measures and Data Issues

NIH’s progress toward meeting this goal has been assessed by a working group of the Advisory Committee to the Director (ACD), NIH. The GPRA Assessment Working Group was composed

of members of the ACD, the NIH's Council of Public Representatives (COPR), and selected members of the Institute and Center (IC) national advisory councils.

The assessment of NIH's research was based on data provided by the ICs (science advances, science capsules, and stories of discovery, as well as research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. Key references were provided for all science advances, science capsules, and stories of discovery. NIH also provided copies of full articles to the assessment working group whenever requested. (For a further discussion of this assessment process and the members of the Working Group, see Appendix 1).

The criteria that were developed and used to assess the outcomes of NIH research under goal d in FY 2001 are as follows:

The NIH biomedical research enterprise *has successfully met this goal* when its research yields new or improved methods for diagnosing disease and disability, and the methods are published and/or disseminated or made available to appropriate populations.

The NIH biomedical research enterprise *has substantially exceeded this goal* when, in addition to fulfilling the criteria under *successfully met*, any of the following applies:

- New findings demonstrate potential to lead/contribute to the development of new and improved diagnostics.

- Diagnostics improve health care and/or quality of life. This includes new or improved diagnostic tools that are more sensitive and accurate; allow diagnosis or detection at an early/earlier stage; enable early/earlier treatment or preventive interventions; predict future susceptibility to disease/disability; and/or less invasive, painful, and/or costly than current techniques.

- Diagnostic methods are applicable to other disciplines, areas of research, or diseases.

The NIH biomedical research enterprise *has not met this goal* when its research fails to yield new findings related biological functions and behavior, or when new findings are not published and/or disseminated.

Goal e) Develop new or improved methods for treating disease and disability.

The development of new treatments for disease is often viewed as the culmination of many years of collaborative effort on the part of the research community. However, the search for treatments actually forms part of a larger knowledge loop. In addition to enhancing quality of life for patients, the search for new treatments often illuminates understanding of fundamental biochemical and molecular processes. Conversely, researchers unraveling the basic mechanisms of complex disease states discover new approaches to treatment. This year, researchers have developed many new and improved strategies for treating disease states, and in the process, they have made significant contributions to the realms of basic science.

As the overall life expectancy increases for United States citizens, researchers have accelerated efforts on diseases associated with aging, such as Alzheimer's Disease (AD). Alzheimer's disease is characterized by the deposition of plaques in the brain, and this year researchers have investigated the mechanisms controlling plaque formation in order to suggest potential treatment strategies for this disorder. As researchers and clinicians respond to increases in the longevity and productivity levels of the overall population, research on AD has large-scale ramifications for the entire nation.

While folklore has supplied popular remedies and treatments, herbal remedies and non-traditional therapies have recently been subsumed into a category of treatments known as "alternative medicine." This year, NIH-sponsored researchers have discovered that these alternative approaches often complement existing treatment paradigms. Moreover, researchers have subjected these remedies to rigorous clinical study in order to elucidate their mechanisms of action. In some cases, researchers have questioned the validity of popularly-held beliefs about such common herbal remedies as St. John's Wort. In all cases, however, research on alternative treatments has important ramifications for the general public, and investigators have used such approaches to examine new treatment modalities as well as to question commonly-held tenets.

As scientists unlock the mysteries of the genome, genetically-based therapies become viable options for treatment. This year, researchers have used direct, localized gene injection to restore blood vessel and tissue growth and to restore vision in animal models. Also, NIH-funded researchers have provided hope for future transplant patients by demonstrating that gene therapy helps to prevent organ rejection following transplant in an animal model. Moreover, recombinant immunotoxins, antibodies genetically engineered to deliver a deadly toxin to tumors, may represent a new weapon in the clinician's arsenal. Finally, NIH-funded scientists have investigated the roles of transcription factors in the onset of certain diseases, suggesting a therapeutic strategy aimed at mediating the function of such compounds.

Although every approach to therapy can technically be described as "novel," scientists have designed several new strategies that Committee Members felt were truly ground breaking. For example, researchers have recently created peptide "nanotubes" that stack atop each other to act as antibiotics by puncturing bacterial membranes. Also, investigators have shown that enzyme

replacement may be a viable paradigm for treatment, as direct infusion of a recombinant enzyme has been demonstrated successful in treating the lysosomal storage disorder, Fabry's disease. Finally, researchers have demonstrated that short pieces of DNA carrying Auger-electron emitting radioisotopes may be deployed to target and "knock out" particular genes. Although still in developmental stages, each of these approaches holds promise for widespread future application.

In addition to these novel approaches, researchers have discovered numerous new uses for currently-approved drugs. From the use of L-arginine supplements to enhance nitric oxide production in patients with sickle cell disease to the application of xylitol, a sugar prescribed to prevent dental caries and acute ear infections, for infection control in cystic fibrosis, old drugs have found numerous new applications in the past year. Treatments based on such strategies illuminate existing knowledge as well as chart new territory.

In addition to drug-based therapies, NIH-sponsored researchers have successfully employed behavioral therapies as interventions for the treatment of pain, insomnia, eating disorders, and depression. In certain instances, investigators have demonstrated that a behavioral modification may complement an existing pharmacologic intervention. In other cases, the behavioral therapy provides an alternative to medicinal application. This year, NIH-sponsored researchers have treated these disorders holistically, thus providing new insight into the interplay between behavior and biology in the treatment of disease.

From standard-of-care issues for individual patients to world health concerns, NIH-sponsored research has forged many new paths for the treatment and control of numerous diseases. In addition to providing novel approaches to and a refined understanding of treatment paradigms, this research lays the groundwork for further investigations designed to improve the quality of life for patients worldwide.

Annual Performance	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Progress in developing (or facilitating the private sector's development of) new or improved treatments that expand therapy options; improve the length and quality of life; and/or are more cost effective -- and which reflect NIH responsiveness to emerging health needs, scientific opportunities, and new technologies.	★	★	★		

Note: This goal will be combined with goal d (p. 106) for FY 2002 and beyond.

★ Target Substantially Exceeded	◆ Target Successfully Met	◇ Target Active	✖ Target Not Met

Summary of Performance Results

- **NIH effective in stimulating quality research**. The NIH's institutes and centers submitted 142 science advances, science capsules, and stories of discovery (tabulated at the end of this

section) under goal e for FY 2001. In the judgment of the assessment working group, the NIH has "substantially" exceeded its target in developing new or improved instruments and technologies for use in research and medicine (see Performance Assessment Approach criteria above for "substantially exceeding" goal).

Without exception, the Working Group had an abundance of positive comments for the NIH-funded research projects described in the GPRA assessment materials. In most cases, reviewers expressed concern about only one study (if any). A member praised the NIH by noting that this collection of scientific research and the novel applications to disease treatment was "astounding." Another member reiterated the committee's consensus that the NIH has been effective in stimulating quality research.

Commenting not only on the included examples but on the vast number of successful studies not chosen for inclusion, a reviewer noted that "the effectiveness of the NIH in stimulating very important research with tremendous implications for the health of the country has, overall, been exceeded." Although the results represent the fruits of continuing studies, one reviewer noted that the results presented in the report provide a snapshot of the ongoing research and indicate that the country "gets a real return on its investment."

In FY 2000, the Working Group concluded that NIH had substantially exceeded the goal. Many of the advances presented showed that NIH-funded research had improved the understanding of basic biological processes critical to the development of therapies and had led to new or improved treatments that improved health care and the quality of life. These advances ranged from novel gene or cell-based techniques, to alternative or low-technology approaches that were simple and cost-effective. The new or potential treatments were often more effective, had fewer side effects, and relieved pain and suffering. Moreover, many have of these treatments have the potential to reduce costs and improve the quality of treatment. The Working Group emphasized that, in many instances, NIH was indispensable to the development of these treatments, because the lack of a financial payoff sufficient to attract private sector interest. The Working Group also emphasized that NIH's contributions to developing new or improved approaches to treating disease and disability are in reality much greater than what appears in the advances provided, because the development of many drugs and devices attributed to the private sector is undoubtedly dependent on years of NIH-supported research.

In FY 1999, the Working Group concluded that the outcomes demonstrated significant progress in the development of new or improved approaches for treating disease and disability. The research outcomes also signify NIH's responsiveness to health needs, scientific opportunities, and development and utilization of new technologies. The new or improved approaches to treatment that have or will arise from this research offer new or expanded treatment options and improved length and/or quality of life for patients. In addition, they may provide more cost-effective strategies for treating disease and disability. In their discussion, members of the Working Group identified a number of important themes or categories of research outcomes relating to treatments, discussed the significance of these types of findings, and highlighted a number of research outcomes that they judged to be especially noteworthy.

Research Outcomes and Their Significance

The assessment working group highlighted a number of significant research outcomes that substantially exceeded the assessment criteria for goal e. For convenience, the research outcomes are divided into some broad themes and will be discussed in some details below.

Research with Implications for the Treatment of Alzheimer's disease (AD)

One of the major hallmarks of AD is the appearance of plaques composed primarily of amyloid β-peptide (Aβ) in the brain. NIH-funded researchers have employed several strategies for controlling plaque formation and deposition as potential treatments for AD. For example, researchers have demonstrated recently that a copper/zinc chelator (a molecule that binds copper/zinc), clioquinol, reduces amyloid accumulation in the brains of transgenic mice– developed as a model for AD.

Using a different strategy, investigators have also developed a chemically-modified type of antisense molecule directed against amyloid β-peptide that reverses learning and memory defects in mice with an AD-like disorder. Antisense therapy involves introducing a molecule that is the exact complement for RNA coding for a harmful protein, thus "locking up" the RNA and preventing protein production.

Researchers have also investigated the steps preceding plaque formation in the progression of AD. A recent study has demonstrated that phenserine, originally developed to increase levels of acetylcholine, can reduce levels of β-amyloid precursor protein (β-APP) thought crucial for plaque formation in the brains of patients with AD. In addition to identifying a new drug target for AD, this study provides insight into the design, development, and synthesis of agents that may regulate optimally and safely β-APP and Aβ levels in the brain. Also, researchers have shown that particular components of the brain's inflammatory response to the cytokine transforming growth factor-β1 (TGF-β1) may act to reduce, rather than elevate, plaque levels in brain tissue of transgenic mice. Better understanding of this process could lead to the development of treatments for AD as well as for the hemorrhage that can occur with vascular disease and stroke.

Investigators have also discovered that the condition of depressed AD patients improved following administration of the anti-depressant sertraline, thus enhancing the quality of life for AD sufferers. The Working Group agreed that these studies have large-scale ramifications for the nation as a whole, as researchers and clinicians respond to increases in the longevity and productivity levels of the overall population.

Over-the-Counter Therapies and Popular Remedies

The Working Group discussed several studies that focused on the popular herbal remedy, St. John's Wort. St. John's Wort is advertised as a mood enhancing drug having anti-depressant qualities. However, the efficacy of this remedy has been questioned in numerous recent studies.

In one report, researchers concluded that St. John's Wort may interfere with the effectiveness of some prescription medicines, and individuals should therefore use the herbal remedy with caution.

Working Group members commended researchers for the rigor with which they conducted the clinical trial, stressing that rigorous, double-blind studies are necessary to ascertain the effectiveness of "alternative" medicines. However, results from another study suggested that St. John's Wort does not interfere with actions of the anticonvulsant drug carbamazepine. Group members cited these somewhat contradictory results as evidence that more studies must be completed before St. John's Wort may be validated as a therapeutic intervention.

In addition to the St. John's Wort studies, group members also discussed two recent significant investigations on over-the-counter pharmaceuticals. The first study revealed that the actual concentrations of ginseng in commercially-available dietary supplements differ widely from the values stated on the product labels. This discovery suggests that careful characterization and standardization of herbal products are necessary for the design and evaluation of studies using those products, and Working Group members highlighted this study as an argument for the importance of truth-in-advertising from a public health perspective.

The second study evaluated eight botanical preparations popular for the treatment of menopausal symptoms and demonstrated that three–red clover, hops, and chasteberry–showed significant estrogenic activity. Although this study suggests that these herbs may supplement the decreased estrogen in menopausal women, additional studies are required to investigate side-effects and to compare the herbal treatments with conventional estrogen-replacement therapy.

Finally, a recent NCI study showed that a diet low in fat and high in fiber, fruit, and vegetables did not reduce the risk of recurrent colorectal adenomas. The Working Group noted that although the study had limitations, the ramifications are important for the general public due to commonly accepted dietary beliefs and habits.

Genetic Bases of Drug Therapy

Several recent studies have investigated genetically-based strategies for drug therapy. One study highlighted by the Working Group identified two genetic polymorphisms (forms with slightly different DNA codes) in the drug-metabolizing enzyme CYP2C8, responsible for taxol metabolism in humans. When transferred to the clinic, results from this study may provide a valuable tool in determining the correct and tolerable doses of taxol administration to cancer patients.

Members also noted the development of a recombinant immunotoxin, BL 22, that appears highly efficacious in disease remission in patients with hairy cell leukemia (HCL). A recombinant immunotoxin is an antibody genetically engineered to deliver a deadly toxin to tumors. In a recent Phase I trial, BL 22 was given to sixteen patients who were resistant to chemotherapy with pentostatin and cladribine. Eleven patients achieved complete remission and two achieved partial

remission of HCL, and if these results are confirmed in further trials, BL 22 offers new hope as a therapy for HCL patients.

Researchers have also described a gene therapy approach to restore blood vessels and reverse nerve damage associated with type 1 and type 2 diabetes in animal models. By directly injecting the gene for vascular endothelial growth factor (VEG-F) into the animals' affected limbs, investigators restored blood vessels and reversed nerve damage with no concomitant damage to the kidneys. If this approach can be shown safe in humans, it could prevent many of the 86,000 diabetes-related amputations performed annually, as well as lower hospital costs and decrease patient morbidity.

Transcription factors are proteins that bind to DNA in a highly specific fashion and regulate the expression of groups of genes. Researchers have recently identified one transcription factor, NFATp, that appears to repress cartilage cell growth and differentiation in stem cell populations of adult animals. The successful regeneration of articular cartilage has not been demonstrated, but identifying compounds that block the function of NFATp may prove valuable in achieving sustained differentiation and growth of cartilage from adult stem cell populations, thus serving as a therapeutic intervention in degenerative joint diseases such as osteoarthritis and rheumatoid arthritis.

Group members also pointed to a study in which researchers were able to induce miniature swine to tolerate major histocompatibility complex (MHC)-mismatched kidney transplants by genetically modifying recipient bone marrow. MHC molecules are present on the surface of almost every cell. Since two individuals rarely share a matching set of MHC molecules, tissue rejection usually occurs in solid organ transplants when the recipient's immune system targets the mismatched MHC molecules. In this study, however, recipient animals maintained their transplants for up to three years, suggesting that gene therapy has the potential to prevent graft rejection without long-term immunosuppression.

Recent work suggests that Marfan syndrome, a heritable connective-tissue disorder characterized by dislocation of the ocular lens, long bone overgrowth, and early death due to aortic rupture, results from mutations in the gene for fibrillin-1, a protein found in elastic fibers. This detailed understanding of the pathogenesis of vascular disease in Marfan syndrome suggests that therapeutic strategies aimed at modulation of cellular phenotype and/or inhibition of protease activity may preclude development of aortic disease associated with the disorder.

The genetic therapy study that drew the most attention was a demonstration that gene therapy can restore vision in a canine model of Leber's Congenital Amaurosis (LCA), a human retinal degradation. In the study, researchers provided vision to three dogs born blind by injecting thousands of copies of the normal RPE65 gene directly behind the retina. The dogs exhibited a mutation in the RPE65 gene that is identical to one that causes about 20% of the human LCA cases.

Group members noted that the research is groundbreaking in that it represents one of the earliest viable gene delivery approaches currently in clinical trials. One group member called the study "the most exciting thing happening in our field [ophthalmology] at the moment," and another

noted that it uses a precise animal model of a human disease to treat a condition that does not easily lend itself to other approaches. In addition to being a good story to tell the public about gene therapy, the study indicates how the research foreshadows product development. Moreover, studies like this one help to justify the necessity for animal research while benefiting the animals themselves.

Novel Approaches for New Therapies

The reviewers categorized several recent investigations under the general heading of "novel approaches" to therapy for their innovative designs and/or unique strategies.

In the normal body, certain immune cells release interleukin-2 (IL-2) when threatened, thus triggering a chain reaction stimulating the immune cells to reproduce. This cascade has become the basis for a novel approach to breast cancer therapy involving the generation of "armed" immune cells that attack remaining tumor cells. When scientists incubated a patient's peripheral blood stem cells with IL-2 and re-injected these treated cells into the breast tissue, the "armed" cells stimulated immune cells to attack the tumor cells selectively.

In a recent Phase III study, researchers showed that therapy with IL-2-incubated cells improved patients' survival as compared to standard therapy, thus suggesting a new paradigm for breast cancer management. This paradigm has been extended to patients with metastatic melanoma through the introduction of IL-2 alongside immunization with peptides from the melanoma antigens. As the genes that encode cancer antigens are identified, it has become possible to develop new therapies using active immunization–vaccines–against the antigens. In recent studies, immunization combined with IL-2 has caused cancer regressions in one third of all patients with metastatic melanoma, thus suggesting a novel strategy for disease remission.

Recently, researchers have developed cell-culture screening tests to identify compounds that may prevent the formation and/or help clear cells of abnormal prion aggregates. Prions are infectious proteins that accumulate in the nervous system and produce a fatal neurological disorder characterized by sponge-like holes in the brain. They are responsible for the human disorder, Creutzfeld-Jakob disease, as well as the bovine disease, bovine sponigiform encephalopathy ("mad cow disease").

Branched polyamines, which have been shown to destroy prions in infected cells, cannot pass the blood-brain barrier, thus becoming ineffective against prions in the brain. However, new screening techniques based on computer models of prion structure have identified several promising candidate drugs as well as provided information on rational drug design for pharmaceuticals designed to kill prions.

Scientists have also devised a novel approach to antibiotic drug design by creating "nanotube" peptides from synthetic rings and strings of amino acids. Under proper conditions, these rings stack on top of one another to form tubes, which work as antibiotics by puncturing bacterial membranes. Once punctured, the bacterial cells spill their contents, thus making this strategy particularly useful for treating infections showing resistance to conventional antibiotics.

Researchers have also demonstrated recently that enzyme replacement may be a viable approach for treating the lysosomal storage disorder, Fabry disease. Fabry disease is a rare genetic disorder caused by a deficiency of the enzyme α-galactosidase A, which breaks down the lipid globotriaosylceramide (GL-3). In recent studies, approximately 70% of patients receiving infusions of recombinant α-galactosidase A demonstrated normal GL-3 levels in their kidneys, and remaining patients had lowered levels. One group member commented that these preclinical studies have provided a compound currently approved for marketing in Europe by two companies. Noting that the compound is currently under FDA review and will likely be available as a therapy within the next several years, he stated that "this is an enormously important demonstration of fundamental basic research identifying a disease [for] continuing effect."

Multi-drug resistance is a major impediment in successful cancer chemotherapy. However, scientists have demonstrated that antigene radiotherapy may selectively target disease-related genes in cultured cancer cells. Using short pieces of DNA carrying Auger-electron emitting radioisotopes, researchers have targeted and "knocked out" the human multidrug-resistant gene MDR1 that encodes for a multi-drug transporter responsible for the increased resistance to anti-cancer drug therapies. Although this technology is still in the developmental stage, it holds great potential as an intervention against cancer.

New Uses for Old Drugs

Adults with sickle cell disease (SCD) are deficient in the amino acid L-arginine, a compound that produces nitric oxide (NO). Nitric oxide is involved in numerous biological processes including blood vessel dilation and prevention of inter-cell adherence. In addition to being safer and more easily administered than inhaled NO, L-arginine supplements have been demonstrated to increase NO production in patients with sickle cell disease. Thus, these supplements may prove a valuable treatment option for severely ill SCD patients.

A recent study has shown that bisphosphonates, a class of drugs with FDA approval for the treatment of osteoporosis and other bone disorders, may also be useful in the treatment of parasitic diseases such as malaria, Chagas' disease, leishmaniasis, and AIDS-related infections. Researchers have demonstrated that these compounds block a key step in parasite metabolism, and they have been successful in curing certain types of leishmaniases in mice models. If they can be shown to have similar effects in humans, these drugs may have widespread use for disease control in Third World countries.

Diabetes is a chronic disease characterized either by an inability to produce insulin (type 1 diabetes) or by the body's inability to use its own insulin (type 2 diabetes). Insulin resistance and compensatory excessive production of insulin become a cycle for the diabetic patient. However, a recent study has demonstrated that high blood sugar and insulin levels in severely insulin-resistant rats and mice may be reversed through administration of high doses of aspirin and sodium salicylate. In addition to potential improvements in treatment, this study illuminates some of the mechanisms underlying the pathogenesis of insulin resistance.

Current osteoporosis therapies work by reducing bone turnover, although they produce only modest increases in bone mass and do not fully reduce fracture risk. However, researchers have demonstrated that bone loss may be reversed in osteoporotic women through daily parathyroid hormone injections. In a separate study, investigators have produced a mouse strain with a receptor for parathyroid hormone that is always "turned on," whether or not the hormone is present. Analysis of the types of bone cells present in these mice lends insight into the mechanism by which parathyroid hormone affects bone regeneration and dissolution. These studies demonstrate the efficacy of parathyroid hormone as a potential treatment for bone loss due to osteoporosis.

A life-threatening consequence of upper cervical spinal cord injury is the interruption of respiratory pathways. Currently, mechanical ventilators provide the primary means of treating spinal cord-injured patients who can not breathe on their own, although this therapy leads to a sense of isolation and a loss of independence. Recently, however, investigators demonstrated the recovery of breathing function in spinal cord-injured rodents through the administration of theophylline to activate alternative respiratory motor pathways. Theophylline significantly increases the speed at which the brainstem reestablishes communication with the diaphragm following spinal cord injury, and this therapy has ramifications for both the survival and the quality of life for spinal cord-injured patients.

Patients with systemic lupus erythematosus (SLE) display an imbalance in certain types of T-lymphocytes, causing elevated production of the cell-surface compund CD154 and the immunoregulatory substance interleukin-10 (IL-10) and decreased production of interferon-γ (IFN-γ). However, researchers have recently demonstrated that trichostatin A, an inhibitor of an enzyme involved in histone modification, significantly reduces expression of CD154 and IL-10 while elevating production of IFN-γ in the lymphocytes of SLE patients. This study suggests that trichostatin A may be a candidate for the treatment of SLE.

Bacterial infection in respiratory tissues represents a major symptom in the onset of cystic fibrosis (CF). A recent report suggests that xylitol, a sugar reported to prevent dental caries and acute ear infections, may offer protection against bacteria that would otherwise infect cystic fibrosis patients. By lowering the salt concentration on airway surfaces, xylitol enhances the airway's innate anti-bacterial defense system and represents a promising avenue for design of therapuetics to prevent or slow the onset of CF-related bacterial infection. One group member noted that this study had added relevance as the first attempt to address clinically whether or not high salt concentration is the determining factor in the success of such treatment.

Highly active antiretroviral therapy (HAART), which uses a combination of several antiretroviral drugs, has dramatically improved the long-term prognosis for individuals infected with human immunodeficiency virus (HIV). However, the antiretroviral drugs produce toxic side-effects, and investigators have explored structured treatment interruptions (STIs) as a way to alleviate these side-effects. A recent study demonstrated that implementing STIs shortly after HIV infection is as effective as continuous HAART to control HIV virus replication. In addition to improving the quality of life for HIV patients, this study demonstrates how improvements to existing treatments alter perceptions of current treatments.

Additions to Existing Knowledge

Group members noted three recent studies that may significantly restructure future dental therapy. First, scientists recently reported that propolis, a resinous beehive product, significantly reduces dental plaque formation by inhibiting glucosyltransferase C from synthesizing glucans from sucrose. Second, researchers investigating the mechanisms of plaque formation have discovered that oral bacteria involved in the formation of dental plaque "communicate" with one another in a process whose mediation is not completely understood. Finally, investigators have identified and characterized stem cells in dental pulp from adult human teeth that give rise to odontoblasts. Odontoblasts generate reparative dentin damaged by injury or disease, and these stem cells may have potential to regenerate new teeth in the future.

Inflammatory pain results from a complex cascade of events, and a recent study has elucidated an important step in the brain's perception of pain during local inflammation. Researchers have identified a cascade of steps involving the enzyme COX-2 and the subsequent production of prostaglandins that affect pain "signals" in the brain. However, the brain's pain signaling pathway is distinct from that at the local site of inflammation. Thus, development of drugs that interfere with the brain's pain signaling pathway should lead to more effective control of inflammatory pain.

Breast cancer is estimated to affect one of every eight women. Currently, there is concern that hormone replacement therapy (HRT) with estrogen, which helps to alleviate the symptoms of menopause, may place older women at greater risk for breast cancer. In recent studies with primate models, estrogen has been shown to promote breast tissue growth, but the male sex hormone testosterone significantly curtails estrogen's growth-promoting effects. These results suggest that combined estrogen/testosterone replacement therapy may reduce the risk of breast cancer associated with estrogen replacement.

Lupus is an autoimmune disease that may affect many parts of the body including the joints, skin, kidneys, heart, lungs, blood vessels and brain. Potent immunosuppressive drugs are often the only effective treatment to control lupus, but these drugs have their own harmful side effects. However, researchers have recently discovered that consensus peptide, a synthetic protein, interferes with the lupus autoimmune response and therefore delays the onset of kidney damage in mouse models. Consensus peptide effectively blocked the auto-immune response even after the disease was present in the mice, suggesting that a similar therapeutic strategy may be useful for humans.

Finally, members highlighted several studies that prove valuable for their methodologies and the contributions they make to basic research. These include three recent reports that help to illuminate the roles of the enzyme p38 and the p53 gene in the initiation of cancer. A fourth study demonstrated that interleukin 15 (IL-15) may play a role in some leukemias. Elucidation of portions of these tumor pathways represents a key basic research component that may provide strategies for treatment design.

Behavioral Therapies

The Working Group cited several behavioral-based therapeutic interventions for the treatment of pain, insomnia, depression, and eating disorders.

First, a recent study has demonstrated the success of a sleep-oriented cognitive behavioral therapy as an efficacious intervention for persistent primary insomnia. Second, researchers have shown that a combination of relaxation and music can reduce pain during a post-operative period. Third, a recent trial demonstrated that cognitive behavioral therapy is superior to interpersonal therapy for the treatment of the eating disorder bulimia nervosa. Finally, a recent report showed the efficacy of eight months of continuation-phase cognitive therapy to reduce relapse in patients with major depressive disorder. In all of these cases, group members commented on the utility of funding behavioral research as a way to discover new therapies.

However, one recent study suggesting that women have a greater tendency than men to catastrophize pain associated with osteoarthritis generated controversy with group members. One member objected to the hypothesis as over-simplified and likely to promote a hasty conclusion. As evidence, she cited results from other NIH-sponsored researchers investigating the complexities of the human mu opioid system, which serves as the brain's natural "painkiller" system. The hormonal mediation involved in the pain response is complex and not fully elucidated, thus suggesting that the response involves more than simple "catastrophizing" of the situation.

World Health Issues

Group members highlighted two studies having immediate world health implications. The first, a meta-analysis of previous studies, demonstrated that a low-cost dietary zinc supplement improves immune system function in children in Third World countries. Moreover, the analysis showed that the zinc supplement reduced the incidence of diarrhea, dysentery, and pneumonia. In addition, children who received the zinc supplement simultaneously with oral hydration therapy for diarrhea had a 42% lower rate of treatment failure or death compared to children who received only oral hydration therapy. The second study revealed that poverty, not ethnicity, is the key factor in predicting early mortality in patients suffering from systemic lupus erythematosus (SLE). The study was groundbreaking in that it was the first to study involving simultaneously Hispanic, African-American, and Caucasian ethnic groups with SLE.

Quality of Life Issues

Reviewers commented that research breakthroughs have affected the standard-of-care and the quality of life for both large and small target populations. For example, several papers examine the role of inhaled corticosteroids in the treatment of the relatively common disorders, childhood asthma and chronic obstructive pulmonary disease (COPD). For children with asthma, the Childhood Asthma Management Program Research Group demonstrated that the inhaled

corticosteroid budesonide proved superior in safety and efficacy to the inhaled non-corticosteroidal anti-inflammatory drug nedocromil in a recent long-term clinical trial.

However, for COPD, results from a recent clinical trial by the Lung Health Study Research Group demonstrate that treatment with inhaled corticosteroids failed to slow progression of COPD. While reducing symptoms, inhaled corticosteroids did not modify the course of the disease, and benefits associated with use should be weighed against potential long-term side effects, such as bone loss.

Group members addressed two studies that relate to treatments for heart failure. The first of these studies, the SHOCK Trial, demonstrated that patients under 75 years of age who receive revascularization immediately after developing cardiogenic shock are significantly more likely to be alive one year after their heart attacks than those who do not. Results from a second study, the Beta-Blocker Evaluation of Survival Trial (BEST), indicate that the beta-blocker bucindolol does not increase survival for patients with moderate to severe heart failure. Moreover, the study revealed that the effects of bucindolol varied with race; black patients received no benefit from the drug, while non-black patients treated with the drug lived longer. These studies were cited for their two-fold importance: they address a ubiquitous problem and have relevance to a large population of patients. Moreover, these studies deal rigorously with treatment paradigms previously addressed with insufficient rigor.

Members also noted several studies that may enhance the standard-of-care for select cancer patients. First, a recent trial demonstrated similar survival rates for radiation and eye removal in patients with ocular melanoma. Although this condition is relatively rare, this study settles an ongoing debate in the ophthalmologic community while providing the patient with options that enhance quality of life. Also, a recent study determined conclusively that cyclophosphamide was a "dangerous" alternative to the more-expensive traditional antithymocyte globulin (ATG) treatment for patients with severe aplastic anemia (SAA). Although SAA sufferers also comprise a relatively small target population, this study has great ramifications for patients receiving these two therapies. Finally, results from a recent clinical trial suggest that nephrectomy increases the survival rate for patients with metastatic renal cell cancer. The implications of this study define a new standard-of-care for patients with kidney cancer.

Stories of Discovery

Members were charged with discussing the most groundbreaking stories of discovery, and their comments are summarized below.

Several participants commented on the NIH's continuing effort to make research information available to the public, and two developments were cited as groundbreaking for sharing and disseminating information. The first of these, the NIH human genome public information resource GenBank, has accelerated gene disease discovery. The second development, the MEDLINE and MEDLINEplus archival systems, has allowed the public to retrieve published research findings on any biomedical subject in the literature.

Approximately 30% of the 400 million annual MEDLINE searches are conducted by consumers. One participant commended the NIH for its developments and addenda to these databases, which have "exploded the potential for sharing information worldwide." He also commented on the large quantity of free information made available through these databases. Members also praised the National Heart, Lung, and Blood Institute (NHLBI) website, which created a tremendous level of excitement among disparate groups related to heart, lung, and blood diseases when it was made available to the public.

Participants also highlighted several other stories of discovery. For instance, investigators have recently discovered the first gene shown to confer susceptibility to Crohn's disease, a debilitating form of inflammatory bowel disease. In addition to providing insight into a disease that affects an estimated 500,000 Americans, this study reiterates the value of using mouse models for genetic research.

One member commented on the value of the NIH's Pediatric Pharmacology Research Unit (PPRU) network, which demonstrates that studies of drugs can be ethically and efficiently conducted in children. She commented that the dosage and tailoring of drugs for children has traditionally lagged far behind that for adults, and the PPRU and the pediatric provisions of the 1997 Food and Drug Administration Modernization Act (FDAMA) have greatly assisted pediatric research.

Finally, one participant mentioned the story of GleevecTM, a promising drug approved this year for the treatment of the blood cancer, chronic myelogenous leukemia (CML). A targeted agent that hones in on molecules specific to cancer cells, GleevecTM represents the fruition of more than forty years of step-wise research. Consequently, the GleevecTM story illustrates the actual process by which research has provided investigators with real molecular targets for drug development within the last few decades.

Verification/Validation of Performance Measures and Data Issues

NIH's progress toward meeting this goal has been assessed by a working group of the Advisory Committee to the Director (ACD), NIH. The GPRA Assessment Working Group was composed of members of the ACD, the NIH's Council of Public Representatives (COPR), and selected members of the Institute and Center (IC) national advisory councils.

The assessment of NIH's research was based on data provided by the ICs (science advances, science capsules, and stories of discovery, as well as research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. (Key references were provided for all science advances, science capsules, and stories of discovery. NIH also provided copies of full articles to the assessment working group whenever requested. (For a further discussion of this assessment process and the members of the Working Group, see Appendix 1).

The criteria that were developed and used to assess the outcomes of NIH research under goal e in FY 2001 are as follows:

The NIH biomedical research enterprise has successfully met this goal when its research yields new or improved instruments and technologies for use in research and medicine, and the instruments and technologies are published and/or disseminated or made available to appropriate populations.

The NIH biomedical research enterprise has substantially exceeded this goal when, in addition to fulfilling the criteria under successfully met, any of the following applies:

- New findings demonstrate potential to lead/contribute to the development of new and improved treatments.

- New or improved treatments improve health care and/or quality of life. This includes treatments that are more effective or have fewer side effects; relieve suffering; are more cost-effective; are less invasive, painful, and/or costly than current methods; effect a cure or remission of disease; and/or restore/increase physical function/activity.

- Treatment approaches are applicable to other disciplines, areas of research, or diseases.

The NIH biomedical research enterprise has not met this goal when its research fails to yield new findings related biological functions and behavior, or when new findings are not published and/or disseminated.

Goal f) Develop critical genomic resources, including the DNA sequences of the human genome and the genomes of important model organisms and disease-causing microorganisms.

Human Genome Project

From its beginning in 1990, the Human Genome Project (HGP) has enjoyed significant success. In recent months, with the publication of the initial sequence and analysis of the human genome, those successes included milestones of historic proportions. From the onset, a major goal of the Human Genome Project has been to sequence, or read, each of the approximately 3 billion bases in the human genetic instruction book. Determining the complete genetic blueprint of humans will greatly accelerate the identification of the genes embedded in this genetic code that underlie many human diseases, including complex diseases that represent the greatest health burden to the U.S. population. Identifying those genes is the first step to a more profound understanding of the biological basis of disease and this, in turn, will lead to much more effective and inexpensive ways to diagnosis, treat and prevent disease.

Many of the project's initial goals have been achieved, including building maps to localize and order the position of genes in both the human and mouse genomes, and sequencing the genomes of model organisms including the bacterium *E. coli*, baker's yeast, and the roundworm *C. elegans*. In addition, sequencing the genome of the fruit fly (*Drosophila melanogaster*) was completed during FY 2000. The ability to compare the sequence of genes across multiple species and develop model systems in simpler organisms will significantly enhance the ability of researchers to identify the functional roles of the encoded proteins and thereby contribute to a better understanding of the molecular basis for human health and disease.

The basic building block of DNA is the nucleotide, and DNA consists of a string of the four nucleotides adenine, cytosine, guanine and thymine (A, C, G, T). Human genes may exist in many different forms, some of them differing only by a single A, C, G, or T. When such minor variations, known as mutations, occur in regions that instruct the production of a specific protein, an altered protein may be formed which may lead to a change in the normal functioning of the human body and which may manifest itself as disease. Additional research efforts will focus on determining the location and function of these genetic variations, with the goal of correlating specific mutations with clinical disease manifestations. Such information is invaluable to medical research and practice—allowing the identification of those at risk for disease, and contributing to the development of rational treatment and preventive strategies. Such precise genetic information may also permit the development of individualized therapies, a burgeoning field known as pharmacogenomics which utilizes genetic information to predict which patients will be most likely to respond favorably to a particular therapeutic drug.

Based on the success of a three-year pilot project, an international consortium, with the U.S. taking the lead, launched the full-scale effort to sequence the human genome in March 1999. On November 17, 1999, the consortium deposited the one-billionth base pair of the human genome into the public database, GenBank, and on March 23, 2000, the consortium deposited the second

billionth base pair. This reflects the remarkable acceleration of human genome sequence production -- it took 4 years to deposit the first billion base pairs of human genome sequence, and only 4 months to deposit the second billion base pairs! Achieving these important milestones affirmed the success of the transition from the pilot to the full-scale production sequencing.

A series of momentous scientific achievements were accomplished in FY 2000 and FY 2001. In December 1999 the complete sequence of chromosome 22 was published in *Nature*, and in May 2000, the complete sequence of chromosome 21 was published in *Nature*. The genome sequence of the most complex model organism to date, the fruit fly, *Drosophila melanogaster*, was published in March 2000 in *Science*. Capping a remarkable series of successes, the international consortium published the initial sequence and analysis of the working draft of the human genome in *Nature* on 15 February 2001. This "working draft" represents 90% coverage of the human genome with at least 99% accuracy. This combined data set of maps and sequence has already accelerated the identification of over a hundred genes that are associated with disease and will serve as a valuable resource for the genetics research community. The consortium now turns in earnest to generating the "finished" human genome sequence, a process that involves closing all remaining gaps and ensuring that all regions of the genome amenable to sequencing meet the consortium's high standards for quality and completion. With the sequencing capacity developed by the international sequencing consortium, it is now also possible to pursue large scale sequencing of the genomes of other vertebrates, including the mouse, rat, and zebrafish. Comparisons between these other genome sequences and the human will be of enormous utility in understanding the functions of human genes and their role in health and disease.

Genomes of Pathogenic Microbes

NIH also is working to sequence the entire genomes of pathogenic microbes and invertebrate vectors of infectious diseases. Worldwide, infectious diseases are the leading cause death for children and young adults, and the second largest cause of death overall. In the United States, infectious diseases are the third ranking killer. Pathogen gene sequencing efforts are enabling scientists to locate genes that may lead to potential new vaccine candidates and drug targets so that infectious diseases can be prevented and treated. In addition, knowing a pathogen's genetic sequence will help researchers better understand how mechanisms of pathogenesis and pathogen mutation contribute to drug resistance. Many medically important microbes have been sequenced including the bacteria that cause tuberculosis, gonorrhea, chlamydia, and cholera and the microbes that cause malaria, pneumonia, meningitis, sepsis, dysentery, anthrax, and plague.

To accelerate research on these pathogens, NIH's data release policy for microbial genome sequencing projects requires that grantees obtain approval of their data release plans and deposit sequence data as they are acquired (at a minimum within one month) in specialized, Internet accessible databases including GenBank, which is run by the National Center for Biotechnology Information. Access to the sequence data, prior to its publication in peer-reviewed journals, enables the broader research community to identify genes of interest and to jump-start relevant experimental studies.

For some pathogen genome sequencing projects, for example the malaria parasite, NIH coordinates its support with funding provided by other national and international agencies, including The U.S. Department of Defense, The Burroughs Wellcome Fund, The World Health Organization, and The United Kingdom's Wellcome Trust. In FY 2000, the NIH entered into an agreement with the Defense Advanced Research Project Agency for sequencing the genomes of pathogens of bioterrorist potential. In addition to coordination of funding, these collaborative efforts help to establish quality control, data release, and other standards by which genome projects are evaluated and funded. Moreover, these interactions are promoting the optimal use of the accrued data by relevant microbiologists and infectious disease specialists.

With NIH support, 18 bacterial pathogens and 2 chromosomes of parasitic protozoa already are completely sequenced. That is, every nucleotide has been identified and properly ordered within the genome (see table below). Once completed, the sequences have been annotated and analyzed using sophisticated computer programs to predict gene structure and function. This information serves as the basis for further experimental studies that help to identify the features of the genome that determine the microbe's ability to infect humans and cause disease.

Completed Pathogen and Parasitic Protozoa Chromosome Sequencing Projects

Pathogen	Disease	Year Published
Actinobacillus actinomycetemcomitans	Periodontal diseases	Manuscript in preparation
Chlamydia pneumoniae	Respiratory disease	2000
Chlamydia trachomatis (human strain)	Chlamydia	1998
Chlamydia trachomatis (mouse strain)	Chlamydia	2000
Enterococcus faecalis (strain V583)	Nosocomial infections	Manuscript in preparation
Escherichia coli 0157:H7	Gastritis, hemolytic uremic syndrome	2001
Haemophilus ducreyi	Chancroid	Manuscript in preparation
Leishmania major Chromosome 1	Cutaneous leishmaniasis	1999
Mycobacterium tuberculosis	TB	Manuscript in preparation
Neisseria gonorrhoeae	Gonorrhea	Manuscript in preparation
Plasmodium falciparum Chromosome 2	Malaria	1998
Porphyromonas gingivalis	Periodontal diseases	Manuscript in preparation
Salmonella typhimurium	Food-borne diseases; gastritis	2001*
Staphylococcus aureus (strain COL)	Bacteremia; endocarditis	Manuscript in preparation
Streptococcus pneumoniae	Respiratory disease	2001
Streptococcus pyogenes	Group A strep	2001
Streptococcus mutans	Dental caries	Manuscript in preparation
Treponema pallidum	Syphilis	1998
Ureaplasma urealyticum	Nongonococcal urethritis	2000**
Vibrio cholerae	Cholera	2000

* published in 1st quarter of FY 2002
** published in 1st quarter of FY 2001

As is true for the Human Genome Project, new technologies employing advances in miniaturization, robotics, and fabrication are providing new tools for research on microbial genomes. In pathogen genome sequencing, high-density arrays of microbial DNA segments (gene "chips" and microarrays) are being used to determine how gene expression varies under different conditions, at different stages of infection, and in different isolates of the organism, as well as to discover new drug and vaccine targets. In parallel, advances in protein detection and characterization are enabling scientists to define a pathogen's proteome (the total complement of proteins within a cell) and its metabolome (the entire set of metabolic pathways accomplished by a cell). More powerful computerized databases are being developed to handle all of the sequence, structure, expression, and function information and to disseminate it to the research community.

Overall, NIH supported approximately 47 large-scale genome-sequencing projects for microbial pathogens and invertebrate vectors in FY 2001. In addition, NIH. awarded a contract at the end of FY 2001 for a pathogen functional genomics resource center, which will provide the research community with resources and databases for functional analysis of microbial pathogens and invertebrate vectors of infectious diseases.

NIH is in the process of reviewing its ongoing priorities and policies for the support of large-scale genome projects as well as other genomic related activities with the help of the NIAID Genomics Task Force, a panel of internationally recognized outside experts in the field, and a Blue Ribbon Panel, which met initially in May 1999. It is anticipated that an update of NIH's priorities and policies for large-scale genome projects will be announced on the NIH/NIAID's Pathogen Genomics Web site.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Complete the sequencing of the human genome:					
Reach U.S. annual production rate of human genomic sequence of 90 million base-pairs.	◆				
Reach worldwide annual production rate of human genomic sequence of 220 million base-pairs.	◆				
Total human genomic sequence completed worldwide at the end of FY 1999 at 400 million base-pairs.	◆				
Worldwide effort completes "working draft" of human genome sequence (90% complete, 99% accurate). U.S. contributes two-thirds of that amount, and NIH contributes 85% of U.S. total.		◆			
Finish the sequence of at least one human chromosome.		◆			
Worldwide effort completes "full shotgun" of human genome sequence (95% complete, 99.9% accurate).			◆		
Finish one-third of human genome (accuracy of at least 99.99%).			◆		
Identify 2,500,000 human single nucleotide polymorphisms (SNPs).			◆		
Finish two-thirds of human genome (accuracy of at least 99.99%). NIH grantees will be responsible for half of this target, i.e., one-third of the human genome.				◇	
Obtain full-length clones and sequence data for 20,000 mammalian cDNAs.				◇	
Finish sequencing of the human genome (accuracy of at least 99.99%).					◇
Obtain full-length clones and sequence data for 40,000 mammalian cDNAs.					◇
Sequence the mouse genome:					
Complete 2X depth of coverage toward the working draft of the mouse genome (90% coverage, 99% accurate).			◆		
Complete full shotgun coverage of the sequence of the mouse genome; finish 10% of the mouse genome.				◇	
Complete full shotgun coverage of the mouse genome; finish 40% of the mouse genome (greater than 99.99% accuracy).					◇
Sequence the rat genome:					
Complete 1X depth of coverage toward the working draft of the rat genome (90% coverage, 99% accurate).			◆		
Complete 3X sequence coverage of the rat genome.				◇	

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Sequence the genomes of other model organisms:					
Complete the sequence of the *C. elegans* genome (97 million base-pairs).	◆				
Complete sequence of the genome of *Drosophila melanogaster* (excluding heterochromatin).		◆			
Sequence the genomes of pathogens:					
Complete worldwide sequencing effort of the entire genome of *Plasmodium falciparum*.			◇→	◇	
Complete sequencing effort of five additional bacterial pathogens and five chromosomes of protozoan parasites.			◇→	◇	
Augment existing knowledge of pathogen genomes by initiating sequencing projects for at least six additional genomes (bacterial, fungal, parasitic).			◆		
Initiate pathogen genome sequencing projects for additional NIH priority areas based upon Blue Ribbon Panel Report.				◇	
Initiate pathogen sequencing projects for additional pathogen genomes (bacterial, fungal, and parasitic).					◇
Develop and facilitate access to new technologies for investigating pathogen gene functions and pathogen /host interaction:					
Establish a mechanism to facilitate access to resources, services, and technologies (bioinformatics, scanning, microarrays, genome chips) needed to investigate microbial gene function.				◇	
Develop technologies that assess, display, and query human genome sequence data to facilitate investigation of how the immune system responds during different disease conditions (i.e., infection, transplantation, autoimmune disease, and other diseases).				◇	
Augment the functional analysis of pathogen genome sequences using state-of-the-art technologies, by providing for technology research, development, distribution, and access and supporting functional analysis research.					◇

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **Completing the sequencing of the human genome remains ahead of schedule.** All targets in FYs 1999 through FY 2001 have been met or exceeded. Sequencing the human genome has always been the ultimate goal of the Human Genome Project. Between March 1999 and June 2000, production of human genome sequence skyrocketed. During this time, scientists sequenced 1,000 DNA letters a second--7 days a week, 24 hours a day. The resulting working draft version of the sequence covered more than over 94 percent of the human genome with over one-third in highly accurate finished form. The average accuracy of all of the DNA sequence in this assembly is greater than or equal to 99.9 percent. The International Human Genome Sequencing Consortium published the sequence and initial analysis of the human genome on February 15, 2001. The sequence and analysis was a

remarkable achievement, representing the work of thousands of scientists laboring in 20 HGP-associated genome centers around the globe.

The February analyses and reports represented the end of the beginning of genomics. They described the first look at the entire human genome sequence. But, the genome contains a vast amount of information, and the scientific community has only begun to understand the stories it contains. The effort to fully translate the mountains of raw genetic data into advances that will improve human health will continue to challenge the brightest minds for decades to come.

Because of the enormous value of sequence information to researchers around the world, HGP scientists have placed all DNA sequence data in public databases where it is immediately and freely available with no restrictions on its use or redistribution. The information is scanned daily by tens of thousands of scientists in academia and industry, as well as by commercial database companies providing information services to biotechnologists. More information about the sequencing and analysis of the human genome is available at: http://www.nhgri.nih.gov/genome_sequence.html.

- **Network established for sequencing of the mouse genome.** The Mouse Genome Sequencing Consortium (MGSC) became fully operational in FY2001 and has made rapid progress. NIH is on target to generate a draft quality version of the mouse sequence early in 2002, a more detailed version of the sequence by 2003, and a finished sequence by 2005. As with the human sequence, the data from the mouse project is rapidly released to the public databases and the World Wide Web with no restrictions. The scientific community is using the data set extensively. NHGRI and the MGSC publish the Mouse Genome Monthly newsletter http://mouse.ensembl.org/newsletter/ that is among a number of means developed to keep the community of mouse researchers abreast of the progress of the sequencing of the mouse genome.

- **Network established for sequencing of the rat genome.** NIH is on target to meet its objective to produce a draft quality version of the rat sequence by 2003. The effort became fully operational in FY2001 and has made rapid progress. As with the human sequence, the data from the rat project is rapidly released to the public databases and the World Wide Web with no restrictions. The scientific community is using the data set extensively.

- **Completing the genome sequences of other model organisms was met.** The FY 1999 target and FY 2000 target were both met. In the first quarter of FY 1999, the complete sequence of the *C. elegans* (roundworm) genome was published in *Science*, and in FY 2000, a consortium of publicly funded scientists, in collaboration with a private company (Celera Genomics), published the complete sequence of the *Drosophila melanogaster* (fruit fly) genome.

- **Some pathogen sequencing projects are taking longer than expected while others are ahead of schedule**. The sequencing of chromosomes of protozoan parasites is taking longer than expected. Due to the size and complexity of the genome of *Plasmodium falciparum*, the

parasite that causes malaria, sequencing of this genome has been divided among different institutions under the coordination of the International Malaria Genome Sequencing Consortium. NIH funding has been used to support the sequencing of three of the fourteen chromosomes of *P. falciparum*, specifically chromosomes 2, 10, and 11. The sequence of chromosome 2 has been published and preliminary sequence data and annotation for chromosomes 10 and 11 are available. Worldwide, outstanding progress has been made in sequencing the other chromosomes. The sequence of chromosome 3 has been published and preliminary sequence data and annotation for chromosome14 are available. The complete genome sequence of *P. falciparum* is expected to be published in 2002. The other four protozoan parasite sequencing projects NIH hoped to complete in FY 2001 -- *Giardia lamblia, Leishmania major, Trypanosoma brucei,* and *Trypanosoma cruzi* also still are on-going. However, NIH has completed sequencing more bacterial pathogens than planned. The genome sequences of five bacterial pathogens were published in FY 2001 (*Escherichia coli* O157:H7, *Salmonella typhimurium, Streptococcus pneumoniae, Streptococcus pyogenes*, and *Ureaplasma urealyticum*) and manuscripts are in preparation regarding the sequences of an additional five bacterial pathogens (*Enterococcus faecalis, Haemophilus ducreyi, Mycobacterium tuberculosis, Neisseria gonorrhoeae,* and *Staphylococcus aureus*). Also, NIH has initiated more (nine rather than six) pathogen genome sequencing activities than originally planned -- *Brugia malayi*, *Clostridium perfringens*, *Coccidioides immitis*, *Cryptococcus neoformans,* Group B streptococcus*, Histoplasma capsulatum, Rickettsia rickettsii, Schistosoma mansoni,* and *Toxoplasma gondii.*

- **NIH is developing and facilitating access to new technologies for investigating pathogen functions and pathogen/host interactions.** Results of this effort will be reported beginning in February 2003.

Verification/Validation of Performance Measures and Data Issues

Performance will be measured by demonstrated increases in the pace and progress of genome sequencing, as scheduled in the targets above. Other assessment measures will include the number of sequence records added to GenBank, including assembled genomic sequence, BAC end sequences, and other sequence data, and progress in sequencing full-length human cDNAs. Of historic significance was the publication of "The initial sequencing and analysis of the human" in the 15 February 2001 issue of *Nature* (Volume 409, Issue 6822, pp. 860-921). In addition, raw data can be found in The Trace Archive, a newly established public database operated by the U.S. National Center for Biotechnology Information, http://www.ncbi.nlm.nih.gov/Traces/trace.cgi. This novel type of database was established to make the individual (raw) sequence publicly available.

The FY 2000 U.S. annual production rate of human genomic sequence was 1.3 billion unique base-pairs. The FY 2000 worldwide annual production rate of human genomic sequence was 2.0 billion unique base-pairs. At the end of FY 2000, the total human genomic sequence completed worldwide was 2.9 billion unique base-pairs.

Both finished and draft sequence data for human, mouse, and rat genomes are deposited into the public database, GenBank. Totals and weekly production rates for the human genome are reported on an NIH website. Since September 1, 1999, sequence information submitted to GenBank by the major participants in the Human Genome Project has included quantitative, 'per nucleotide' quality estimates provided by appropriate analytical software; this quality information is also available publicly. Independent assessment of the quality of the sequence data produced under NHGRI funding will be done by a quality assessment process. Evaluations will be publicly available through a website and publication.

Single nucleotide polymorphisms (SNPs) into dbSNP, a freely accessible NIH database at the National Center for Biotechnology Information. Totals are reported on an NIH website: http://www.ncbi.nlm.nih.gov/SNP/overview.html.

Sequence data for the full-length cDNA clones will be deposited into GenBank and identified as part of the Mammalian Gene Collection http://mgc.nci.nih.gov/. Clones will be available to researchers from a central repository.

The sequences of disease-causing microorganisms are deposited in public databases that have Intranet sites and are published. Citations are available for all publications. In addition to sequence data that are deposited in GenBank, http://www.ncbi.nlm.nih.gov/GenBank/ , depositions frequently are made to other public databases, including:

- http://www.tigr.org/tigr-cripts/CMR2/CMRHomePage.spl. (*E. Faecalis and S. aureus*)
- http://genome.wustl.edu/gsc/Projects/S.typhimurium (*S. typhimurium*)
- http://www.genome.ou.edu/gono.html (*N. gonorrhoeae*)
- http://hermes.mbl.edu/baypaul/Giardia-HTML/index2.html (*G. lamblia*)
- http://www.genome.sbri.org/lmjf (*L. major*)
- http://www.plasmodb.org/ (*P. falciparum*)
- http://www.tigr.org/tdb/mdb/tbdb (*T. Brucei*)
- http://wwwcruzi.genpat.uu.se (*T. Cruzi*)
- http://www.tigr.org/tdb/mdb/tcdb/ (*T. Cruzi*)
- http://www.sbri.org/genome (*T. Cruzi*)
- www.tigr.org/tdb/mdb/mdbinprogress.html (*C. perfringens*)
- www.sequence.stanford.edu/group/C.neoformans/index.html (C. neoformans)

Goal g) Develop an AIDS vaccine by 2007.

As the HIV pandemic continues to rage around the world, a safe and effective AIDS vaccine is a global public health imperative. With the expectation that 3 million people will die of HIV/AIDS in 2001, HIV/AIDS is the fourth leading cause of mortality and its impact is going to increase. Worldwide, roughly 5 million people will be infected with HIV during 2001 and 40 million will be living with HIV/AIDS. Over 95 percent of new cases occur in the developing world, mostly among young adults and increasingly in women. About 68 percent and 16 percent of the infections occur in sub-Saharan Africa and South-East Asia, respectively. In seven countries in southern Africa, at least a one in five adults is living with HIV. Moreover, HIV/AIDS is poised to devastate other regions as well. HIV infections are rising faster in Eastern Europe than anywhere else in the world. In the Russian Federation, in 2001, there were 250,000 new HIV infections bringing their total number of people living with HIV to 1 million. Moreover, HIV also continues to have a profound effect on children, with approximately 2.7 million below the age of fifteen expected to be living with the disease by end of 2001.

HIV/AIDS is having a worldwide impact as the number of sick and dying people depletes the skilled workforce in the developing world; as commercial, governmental, educational, and military sectors lose capability and productivity; as families lose wage earners; and as a multitude of children become impoverished orphans. In response to this crisis, the United Nations Security Council declared AIDS an issue of national security, representing a new kind of threat to political stability. A vaccine offers the best hope for halting the HIV pandemic.

In the United States, the number of deaths due to HIV/AIDS has declined substantially in the last decade due primarily to the introduction of antiretroviral drugs. When used in combinations termed highly active antiretroviral therapy or HAART, these drugs can decrease the amount of virus in the body to virtually undetectable levels. But the prolongation of the lives of infected individuals has resulted in more individuals living with the disease. According to the Center for Disease Control (CDC), roughly 800,000 to 900,000 residents the United States are living with HIV/AIDS, with about one third unaware of their HIV positive status. New infections continue at roughly 40,000 per year, with more than half occurring in individuals younger than 25 years of age. HIV/AIDS also continues to disproportionately affect minorities, notably African Americans. In fact, African Americans make up almost 38 percent of all AIDS cases reported in this country even though they represent an estimated 12 percent of the total United States population. For a decade, HIV/AIDS has been the leading cause of death for African American males aged 25-44. In children, African Americans represent almost two-thirds of pediatric cases.

Since the beginning of the epidemic, NIH's comprehensive research program has made significant progress in elucidating the structure of HIV, understanding the role of the immune system in controlling HIV, developing new and improved models for testing candidate vaccines, and in sponsoring and conducting clinical trials.

Late in the summer of 2000, construction of the Dale and Betty Bumpers Vaccine Research Center (VRC) was completed and newly recruited scientists began moving into their laboratories. The VRC was created to conduct a comprehensive program of vaccine research on the NIH intramural campus. The primary focus of the VRC in its first years is a vaccine for AIDS. In October 2001, just a year after construction of the building, the VRC launched clinical testing of their first vaccine. The role of the VRC is to stimulate multi-disciplinary research, from basic and clinical immunology and virology through to vaccine design and production. In addition to the investigations carried out on the NIH campus, the VRC works with scientists in academic, clinical, and industrial laboratories through a program of national and international collaborations. The VRC facilitates the movement of ideas from the broader community into clinical trials by filling the gap between new basic concepts in immunology and initiation of clinical trials through the application of state-of-the-art methods to rational vaccine design. The VRC conceives, designs, and prepares vaccine candidates and performs laboratory analysis, animal testing, and clinical trials on candidates found to be viable.

Complementing the intramural NIH AIDS vaccine effort is an extensive extramural program. In all, ten NIH units have activities to advance progress toward an AIDS vaccine. These activities include a comprehensive Vaccine and Prevention Research Program sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), the investments of the Fogarty International Center (FIC) in training of foreign scientists, work on primate models sponsored by the National Center for Research Resources (NCRR), and considerable basic research relevant to vaccines on the part of the National Cancer Institute (NCI).

In the basic research arena, NIAID's extramural AIDS vaccine research program supports research on novel vaccine concepts, genetic and immunologic variation, mucosal immunity, delivery methods, adjuvants, and correlates of immune protection. At the preclinical level, NIAID's programs include support for the development of new candidate vaccine designs, evaluation in non-human primate models of HIV/AIDS, pilot-lot production, and additional preclinical work required for advancement into human trials. At the clinical level, the program coordinates all phases of clinical trials of candidate AIDS vaccines and supports work to characterize immune responses in vaccinated volunteers.

The NIH Office of AIDS Research has the important role of coordinating efforts across institutes.

Major Activities and Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Design and develop new or improved vaccine strategies and delivery/production technologies:					
Increases in the research portfolio supporting innovative vaccine discovery.	◆				
Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.		◆	◆	◇	◇
Develop and utilize animal models for testing candidate vaccines:					
Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.		◆	◆	◇	◇
Advance clinical research by completing ongoing vaccine trials and initiating new trials:					
Progress in completion of ongoing trials.	◆	◆	◆	◇	◇
Progress in initiation of additional domestic and/or international trials of new or improved concepts and designs, including the progression of promising candidates to larger trials testing vaccine candidates.	◆	◆	◆	◇	◇
Strengthen collaboration:					
Increased interactions between academic investigators and industry, to enhance opportunities for vaccine discovery and product development.	◆				
Progress in collaborating with industry to enhance opportunities for vaccine development.		◆			
Progress in collaborating with scientists in developing countries and with industry to further promote the development of vaccines for world-wide use.			◆	◇	◇

Note: Given the encompassing and long-term nature of research, progress toward this goal is marked by an "annual target" which does not change from year-to-year.

◆ Target Met	◇ Target Active	◇⟶ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **Advances in the design and development of vaccine strategies continue to fuel the pipeline of promising HIV/AIDS vaccine candidates**. In FY 1999, the number and dollar value of awards made for vaccine discovery increased. In FYs 2000 and 2001, notable scientific progress was made, as evidenced by the emergence of new vaccine concepts, the advancement of vaccine concepts into preclinical testing, and promising results in preclinical testing (animal models). Vaccine candidates and concepts evaluated preclinically in FY 2001 include improved DNA vaccines, a stabilized HIV envelope protein, novel viral vectors, and HIV regulatory proteins. There are now over a dozen candidate vaccines advancing toward clinical studies by NIH-funded researchers in academia and the private sector. A couple of the more promising are highlighted below.

DNA vaccines and viral vectors incorporate HIV genes to produce specific HIV proteins that then induce an immune response.

- In a recent study, NIH supported scientists demonstrated that a new HIV DNA vaccine used in combination with a vaccina virus booster vaccine is capable of protecting rhesus monkeys from disease. All vaccinated animals remained clinically healthy while nearly all of the unvaccinated ones developed clinical AIDS several weeks after challenge with virus.

- In another HIV DNA vaccine study, investigators demonstrated that a DNA vaccine combined with an adjuvant (a substance that enhances the immune-stimulating properties of a vaccine) also prevented the onset of clinical AIDS in rhesus monkeys.

A vaccine that does not prevent HIV infection, but that instead slows the course of disease may not only benefit vaccinated individuals, but also could decrease the spread of disease because sufficient lowering of the viral load in HIV-infected individuals has been shown to decrease the transmissibility of the virus. Both HIV DNA vaccine candidates are progressing toward a phase I human trials.

- **NIH has been successful in utilizing animal models for testing candidate vaccines and in making progress toward development of new models**. Existing animal models were utilized in both FY 2000 and FY 2001 to make important progress in the design of vaccine candidates and development of new animal models. Animal models, especially the use on non-human primates, continue to provide valuable information in advancing HIV vaccine research and in testing candidate vaccines. The advances utilized non-human primates in their evaluation of candidate vaccines. In addition to non-human primates, researchers are continuing to develop other animal models. In FY 2001, a number of important studies were published showing progress towards the development of a small animal model for AIDS. The two species that researchers have been focusing on are the rat and the mouse. Recently, NIH-supported investigators overcame some of the barriers to the creation of a functional rat model of HIV. In related studies on a mouse model of HIV, two independent investigators have made progress in identifying human genes required for HIV cellular entry and replication in that species.

  Progress in the utilization of animal models for evaluation of candidate HIV vaccines also was made from a programmatic standpoint. An important mechanism for utilization of animal models is NIH's Simian Vaccine Evaluation Units (SVEU) program. NIH solicited applications from facilities that can continue and expand the capabilities of the current SVEUs. As a result of the solicitation, NIH awarded three new contracts in FY 2001.

- **NIH has advanced clinical research by completing ongoing vaccine trials and initiating new trials.** In FY 1999, four new clinical trials were initiated, and of the seven trials started in prior fiscal years, two more completed accrual. In FY 2000, one new trial began and four ongoing trials were completed. In FY 2001, NIH completed seven clinical trials and initiated

two new phase II vaccine trials, one domestic and the other in the Caribbean and Brazil. These trials are being conducted under the direction of the HIV Vaccine Trials Network.

Trials Completed or Initiated during FY 2001 (10/1/00 – 9/30/01)				
Study	**Phase**	**Vaccines Evaluated**	**Accrual Initiated**	**Accrual Completed**
Completed				
AVEG 027	1	ALVAC vCP205 rgp120 MN	11/97	10/98
AVEG 031	1	Gag-Pol DNA Amended to add vCP205	11/98	2/99
AVEG 032	1	ALVAC vCP205 1 +/- rgp120 SF-2 [4], +/- p24 [4]	8/99	9/99
AVEG 033	1	ALVAC vCP205 + GM-CS F Amended to add Gag- Pol DNA	1/98	6/98
AVEG 034A	1	ALVAC vCP205 or ALVAC vCP1452	9/99	12/99
AVEG 202/ HIVNET 014	2	ALVAC vCP205 +/- rgp120 SF-2[4]	5/97	1/98
HIVNET 007	1	ALVAC vCP205	2/99	8/99
Initiated				
HVTN 203	2	ALVAC vCP1452 +/- rgp120 MN or rgp120 MN/GNE8 (B/B')	12/00	9/01
HIVNET 026	2	ALVAC vCP1452 +/- r rgp120 MN	3/01	--

- **NIH has strengthened collaborations with scientists in developing countries and with industry.** In FY 1999, actions were taken to increase the interaction between academic investigators and industry including a workshop and resource sharing. In FY 2000, several HIV Vaccine Design and Development Team awards were made to promote university-industry collaboration in the development of AIDS vaccines and the HIV Vaccine Trials Network (HVTN), an international network of sites for the conduct of clinical trials of candidate HIV/AIDS vaccines, was established. In FY 2001, a solicitation for additional HIV Vaccine Design and Development Teams was issued, additional contracts with industry for Vaccine Development Resources were awarded, a Cooperative Research and Development Agreement (CRADA) with Merck was established, vaccine related awards were issued under the Comprehensive International Program of Research on AIDS, and a phase II clinical trial started under the auspices of the HVTN.

Verification/Validation of Performance Measures and Data Issues

Précis of science advances will be used to document progress in vaccine strategies, delivery/production technologies, and animal models. The progress in collaborating with scientists in developing countries and with industry will be inferred on the basis of activities to promote such interaction. NIH and NIAID databases provide documentation of these activities. Information from the Statistical Center for HIV/AIDS Research and Prevention (SCHARP) at

the Fred Hutchinson Cancer Research Center, Seattle, Washington will be used to compile a record of the completion of ongoing vaccine trials and the initiation of new trials.

Citations will be available for all science advances considered in the assessment process. NIH and NIAID databases, including Computer Retrieval of Information on Scientific Projects (CRISP) and Scientific Information Management System (SIMS), which are used to track research awards and initiatives, and the contract archives contain objective data on grant and contract awards and on the establishment of initiatives. The electronic archive of the NIH Guide also contains objective data on establishment of initiatives. The SCHARP database on the status of NIH HIV/AIDS vaccine trials maintains data from each of the clinical trial sites.

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2.1.2.2 Communication of Results

Communicating scientific results and health information to the medical research community, health care providers, patients, and the general public has long been recognized as a critical NIH function. Information dissemination helps ensure that the science NIH conducts and supports is applied appropriately – whether by other scientists, health care providers, patients, or the public. Without the flow of information, important scientific findings would languish at the researcher's bench.

The Public Health Service Act of 1944 authorized NIH and the other PHS agencies to collect and make available, through publications and other appropriate means, information relevant to the practical applications of research [Title III, Sec. 301 (1)]. In addition, the legislation that enables and directs the development of NIH programs emphasizes NIH's important role in informing the public about the results of health-related research. Similarly, the authorizing legislation for the NIH Institutes and Centers (ICs) includes "dissemination of health information" as an integral part of each IC's basic mission.

All of the NIH ICs conduct programs to collect, disseminate, and exchange information on medical and biological science, medicine, and health. The National Library of Medicine (NLM), the world's largest medical library, is a component of NIH and works closely with the ICs to ensure the effective communication of research results. NLM has a broad Congressional mandate, not only to collect and organize the literature of the health sciences and to provide information services, but also to develop outreach programs aimed at transferring the latest scientific findings to the scientific community, health professionals, researchers, and the general public worldwide.

To effectively communicate scientific results and health information to a variety of populations, NIH's key challenges are to: 1) increase the audience members' awareness that useful information is available; 2) ensure that they have access to the types of information they need; and 3) improve their understanding of how to use the information. A related challenge is to design communication strategies that will enhance public and provider awareness and understanding of clinical research, and increase their willingness to participate in NIH-sponsored clinical trials.

To address these challenges and enhance the effectiveness of its communication efforts, NIH established five performance goals:

a) Increase awareness of NIH-sponsored research among health care providers to promote research application.

b) Increase awareness of NIH-sponsored research results among racial/ethnic minorities and high risk, underserved, and/or affected publics.

c) Increase awareness of NIH-sponsored research results among the general public.

d) Increase awareness of clinical research and support participation in clinical trials.

e) Establish a Clinical Trials Database, as required by the FDA Modernization Act.

NIH's efforts to achieve these performance goals include developing health education materials and implementing communication campaigns to reach specific audiences with information on significant health problems. Other activities focus on enhancing NIH operations, using techniques such as telehealth technology and consolidated databases, developing web-based tools, and strengthening collaborations with other organizations to improve the communication of research results and increase clinical trial participation. In addition, NIH conducts needs assessments and other evaluation studies as needed to improve communication initiatives within a competitive information environment.

Performance Goal Details - Communication of Results

Goal a) Increase awareness of NIH-sponsored research among health care providers to promote research application.

NIH's research mission - to develop new knowledge that leads to better health - depends on translating research advances into improved patient care. This goal contributes to that translation significantly, because the first step in the "chain of events" in using research results to improve patient care is to ensure that health care providers learn about the latest research findings.

To increase awareness of NIH-sponsored research among health care providers, NIH is concentrating on three major activities: 1) disseminating and evaluating the use of clinical practice guidelines, 2) developing and implementing communication campaigns designed to reach health professionals, and 3) exploring the potential of telemedicine and other technology for improving health care delivery.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Disseminate and evaluate the use of clinical practice guidelines:					
Evaluate the use of clinical practice guidelines on treatment of high blood pressure and high blood cholesterol by physicians who provide care to African-American patients.	◇→	◆			
Evaluate the use of clinical practice guidelines on high blood pressure and obesity.	◇→	◆			
Disseminate and encourage the use of clinical practice guidelines for the treatment of high blood pressure, high blood cholesterol, and other conditions by physicians who provide care to African-American patients.		◆			
Use continuing medical education programs based on the web-based Asthma Management Model System to disseminate and encourage the use of clinical practice guidelines on asthma.			◆		
Collaborate with the National Committee for Quality Assurance to foster implementation of cholesterol clinical practice guidelines.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Develop and implement communication campaigns designed to reach health professionals:					
Use telehealth technology and TV cable networks for education projects with nursing organizations and academic institutions: broadcast select conferences and workshops to nursing organizations and academic institutions and add website components that will allow users to interact on-line with live discussions, conferences, and other types of meetings.		◇→	◆		
Expand the "Not Just Once, But for a Lifetime" mammography campaign to reach health professional organizations, physicians, nurses, and other health and medical practitioners to increase awareness of the importance of mammography screening and the Medicare mammography benefit, and referrals for women, particularly those aged 65 and older.		◇→	◆		
Complete web accessibility for viewing nursing education programs and establish a once-a-month chat room where program directors will be available to answer questions from nursing students and nurse researchers.			◆		
Increase awareness of NIDA-sponsored clinical treatment among health care providers.			◆		
Use a partnership with the American Academy of Family Physicians to increase the knowledge of primary care physicians about the diagnosis and treatment of mental disorders.			◆		
Develop a communications campaign to build support and enhance the recruitment for domestic and international AIDS vaccine trials.				◇	
Explore the potential of information technologies to educate health professionals:					
Fund a series of demonstration projects applying telemedicine and other technology to improve the speed of reaching heart attack victims with lifesaving treatment.		◆			

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **Clinical practice guidelines have been disseminated by NIH via the Internet.** As a means of fostering the use of its clinical practice guidelines on asthma, NIH developed and marketed a comprehensive Internet-based Continuing Medical Education (CME) module covering all aspects of asthma clinical management. By the end of FY 2001, approximately 800 physicians had accessed the module and completed the course for full CME Category I credit. This effort followed NIH's earlier success in disseminating and evaluating the use of clinical practice guidelines. In FY 2000, NIH completed an evaluation of the use of clinical practice guidelines on the treatment of high blood pressure and high blood cholesterol by physicians providing care to African American patients. To disseminate and encourage use of the guidelines, NIH developed model case studies on 11 aspects of treating cardiovascular disease in African Americans. The model case studies were used to develop interactive web-based programs for physicians and nurses, and continuing education credits were offered to participants.

- **NIH reaches health professionals through communication campaigns.** NIH made substantial progress in FY 2001 in reaching health professionals with important health information. The Breast Cancer and Mammography Education program and the National

Institute on Drug Abuse (NIDA) Clinical Trials Network were expanded to reach more health professionals, and NIH used its partnership with the American Academy of Family Physicians to develop training programs on mental disorders. These programs included a monograph on the diagnosis and treatment of depression and a public education campaign to increase awareness of mental health problems and the role of the family physician in managing these problems.

- **NIH continues to explore the potential of telemedicine and other technology for improving health care delivery.** NIH funded ten awards in FY 2000 for demonstration projects, which included investigating the potential of various high tech applications to expedite the delivery of treatment to heart attack patients. NIH also collaborated with two other organizations to develop a videotape series for health care providers on end-of-life care. More recently, NIH has explored how Personal Digital Assistants (PDAs) may be used to provide medical information to health professionals. By the end of FY 2001, over 4,200 users had downloaded the Palm Pilot version of NIH's guidelines for the treatment of asthma.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the successful completion of planned evaluation and dissemination activities and development of model case studies and other training programs for health care providers. NIH uses several means to verify performance data, including statistical reports showing the number of health professionals who have received information materials from NIH, the number of completed and graded tests for CME Category I credit, and analyses of NIH website usage, including downloads of specific NIH tools.

Continuing Medical Education (CME) is part of NHLBI's Asthma Management Model System, a special professional education section on NHLBI's site. Many more physicians have visited the CME site, accessed the course, and possibly registered for Category II credit. However, this use cannot be tracked since Category II does not require the user to return a test for grading.

Goal b) Increase awareness of NIH-sponsored research results among racial/ethnic minorities and high risk, underserved, and/or affected publics.

Many NIH research results apply to particular segments of the public, such as those at greater risk of contracting a specific disease or those who may not visit a health care provider regularly. However, these research results may not reach the populations who are the most likely to benefit from them.

One of NIH's major priorities is to help reduce the striking disparities in the burden of illness and death experienced by certain groups in the U.S., particularly racial/ethnic minorities and other high-risk and underserved populations. The goal of increasing their awareness of NIH-sponsored research results responds to this priority directly. To achieve this goal, NIH focuses on developing and implementing: 1) health education materials for non-English speaking and low-literacy audiences, 2) communication campaigns designed to reach high-risk populations, and 3) communication campaigns on specific health issues.

To reach high-risk populations, NIH develops targeted communication campaigns to disseminate information and resources on diseases and conditions that are more prevalent in certain populations, such as diabetes, drug abuse, and noise-induced hearing loss. Campaigns are designed to reach specific minority groups (e.g., African American, Hispanic, American Indian, and Asian communities), seniors, and other populations at high risk.

NIH also develops broad communication campaigns on a variety of specific health issues, such as sports injury prevention, the health implications of obesity, and eye health.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Develop health education materials for non-English speaking and low-literacy audiences:					
Establish a centralized site on the NIH home page for access to NIH materials in Spanish.	◆				
Evaluate several selected NIH outreach programs: cardiovascular health outreach activities for Latinos.	◆				
As an activity of the NIH Hispanic Communications Initiative (HCI), conduct a Spanish-language "media summit" that will detail strategies for developing continuous and sustainable working partnerships between NIH information offices, national Spanish-language media outlets, and national Hispanic intermediary organizations.		◇→	◆		
Develop and disseminate easy-to-read and Spanish language health education materials on health issues to targeted special populations.		◆			
Expand programs on anxiety disorders and depression to audiences for whom language or literacy are challenges.		◆			
Develop and disseminate Asian language materials communicating the benefits of mammography.				◇	

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Develop and implement communication campaigns designed to reach high-risk populations:					
Develop and implement NIH information, education, and outreach programs on specific health issues: extend the "Back to Sleep Campaign" to minority populations.	◆				
Pursue new outreach and collaboration initiatives to disseminate information and resources on rheumatic diseases in minority populations.		◆			
Develop and implement diabetes awareness campaigns that target minority populations and their health care providers.		◆			
Develop and disseminate motivational messages related to breast and cervical cancer screening to African American, Hispanic, and Asian communities.		◆			
Increase the available information on the benefits of exercise to older people.		◆			
Increase awareness of autoimmune diseases (such as rheumatoid arthritis, lupus, and scleroderma) among minority populations who are disproportionately affected.			◆		
Increase understanding about the seriousness of diabetes and the importance of blood glucose control among African Americans, Asian/Pacific Islanders, and American Indians.			◆		
Increase awareness about how to prevent fully preventable noise-induced hearing loss (WISE EARS! Campaign) among industrial workers, Hispanic/Latino/Latina individuals, and Native American youth and their parents.			◆		
Increase knowledge among Hispanic parents of the effects of drugs on the brain and encourage them to talk with their children about drug abuse.			◆		
Increase awareness of the effects of drug abuse among Native American Indians.			◆		
Provide support and technical assistance to NHLBI's Enhanced Dissemination and Utilization Centers to conduct heart-health education projects in high-risk communities.				◇	
Develop and implement communication campaigns on specific health issues:					
Develop and implement NIH information, education, and outreach programs on specific health issues: Breast Cancer and Mammography Education Program.	◆				
Develop and implement an AIDS vaccine communication campaign to increase awareness of AIDS vaccines before the initiation of a large efficacy trial.			◇→	◇	
Increase awareness of sports injury prevention among parents.			◆		
Develop messages and materials to communicate the health implications of obesity.				◇	
Develop and implement an eye health awareness campaign.				◇	
Implement a campaign to provide information on noise-induced hearing loss.					◇
Use a variety of media approaches (t.v. and radio news inserts, etc.) to communicate the importance of eating 5 fruits and vegetables a day.					◇

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

- **NIH develops and distributes health education materials to non-English speaking audiences.** NIH has successfully met all of its targets to date aimed at reaching non-English speaking and low-literacy audiences. Specifically, NIH established and launched a centralized site on the NIH home page offering access to NIH materials in Spanish. NIH also developed posters about type 2 diabetes that were translated into 11 languages for Asian American and Pacific Islander audiences. In addition, NIH wrote articles for Spanish-language newspapers (with a readership of about 800,000 people), developed a Hispanic/Latino diabetes awareness campaign that included TV public service announcements (PSAs) in Spanish, and distributed Spanish-language booklets on the effects of drugs.

- **NIH reaches high-risk populations through communication campaigns.** NIH has met all of its targets to date to develop and implement communication campaigns for high-risk populations. Specifically, NIH launched five major diabetes education campaigns intended for those populations that suffer disproportionately from the disease—African Americans, American Indians, Asians and Pacific Islanders, and Hispanics/Latinos. NIH also created a coalition of partners ranging from the Indian Health Service to the Migrant Clinicians Networks to carry out an education campaign to help prevent noise-induced hearing loss among industrial workers, Hispanics/Latinos, and American Indian youth and their parents. To enhance its public awareness campaign against drug abuse, NIH developed and distributed booklets, fact sheets, innovative calendars, and radio and television PSAs aimed at Hispanic and American Indian audiences.

- **NIH successfully launched two campaigns to increase awareness on specific health issues.** After implementing the Breast Cancer and Mammography Education Program in FY 1999, NIH continued to develop campaigns addressing specific health issues. For example, NIH collaborated with over 2,700 YMCAs and YWCAs in FY 2001 to educate parents about childhood sports injuries and how to prevent them. The campaign included the development, distribution, and promotion of a fact sheet entitled, *Childhood Sports Injuries and Their Prevention: A Guide for Parents with Ideas for Kids*. NIH also made substantial progress in developing an awareness campaign to accompany the launch of a major AIDS vaccine clinical trial, although the FY 2001 target for this activity was not met on schedule. NIH still needs to complete formative research studies to ascertain current attitudes of the American public about an AIDS vaccine. This essential research phase includes conducting focus groups throughout the country, monitoring media messages and content, and reviewing the literature and materials of similar campaigns. The AIDS vaccine communications campaign will accompany the launch of an AIDS vaccine clinical trial in May 2002.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the successful development of specific health education materials and the development and implementation of planned communication campaigns. NIH uses

several means to verify performance data, including statistical reports showing the number of TV PSAs distributed to and broadcast by television stations, cable stations, and cable systems. Other data sources include reports regarding newspaper placements, NIH website usage, and inquiries to different NIH information clearinghouses.

Goal c) Increase awareness of NIH-sponsored research results among the general public.

NIH disseminates new knowledge resulting from research as broadly as possible to increase public awareness. Often, the public can use information that results from NIH-sponsored research to improve their health and the health of their families. Therefore, the broader the dissemination of selected, widely applicable research results, the greater the number of individuals and families who are likely to benefit. To achieve this goal, NIH is focusing on: 1) enhancing NIH operations to improve the communication of research results. 2) strengthening collaboration with other organizations involved in health communications, 3) developing and implementing communication campaigns on specific health issues, and 4) increasing the public's awareness of specific health issues and the role of NIH.

To improve the communication of research results, NIH is developing an easily navigable website intended for older Americans so they can more easily access health information; it also is planning a process evaluation of the effectiveness of Pap test information materials.

To strengthen collaborations with other organizations involved in health communications, NIH developed relationships with constituency groups nationwide to increase awareness of the latest scientific information about drug abuse and addiction prevention and treatment. In addition, NIH improved public access to health information by ensuring that a medical library in every state is sharing information with public libraries and community organizations. To reach the broadest audience across the nation, NIH uses mass media materials distributed to the print media, cable networks, and broadcast television and radio stations in all 50 states. NIH campaigns on three specific health issues are currently under way to: 1) educate young people about the importance of calcium in their diet, 2) increase the number of people who know the symptoms of stroke and when to seek treatment, and 3) increase awareness among the general public that drug addiction is a brain disease.

Many Americans are unaware that NIH funding and basic research are major factors in almost every U.S. biomedical discovery. To increase public awareness of its crucial role, NIH uses mass media communications as well as promoting direct public access to information. Specific examples include: increasing awareness among the general public about the achievements of publicly funded vision research and increasing the public's understanding of cancer research and its advances. These activities complement targeted campaigns for minority communities, high-risk populations, and members of the public who may have inadequate access to health care.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Enhance NIH operations to improve the communication of research results:					
Implement a system to track customer service interactions, measure response times, and record customer feedback on NLM products and services.	◆				
Provide a single toll-free telephone number to reach NLM customer service staff.	◆				
Complete the restructuring of NIMH's mental health education and information dissemination programs.	◆				
Increase the availability of consumer health information, publications, and reports under NIH's Centralized Consumer Health Information area by 20 percent.	◆				
Increase the usage of NLM's existing catalog-based databases for books, serials, and audiovisuals by 15 percent.		◆			
Increase the number of "health topics" in the web-based MEDLINEplus to 300.		◆			
Ensure that no less than 85 percent of respondents to a customer feedback instrument rate NLM services at least satisfactory.		◆			
Introduce an easily navigable site on the World Wide Web that can increase older adults' awareness of health information and, based on the National Institute on Aging-supported cognitive research findings, enhance the online learning experience for people age 60 and over.				◇	
Perform a process evaluation of the effectiveness of pap test information materials produced in FY 2001.				◇	
Launch three new services to enhance the online health information resource, MEDLINEplus.					◇
Strengthen collaborations with other organizations involved in health communications:					
Strengthen relationships with universities, voluntary health associations, and other organizations that communicate health and scientific information – to expand the options for communicating NIH research results.	◆				
Increase collaboration with professional associations of journalists, science writers, and health communicators to increase their coverage of NIH-funded research results.		◆			
Implement WISE EARS! communications program by developing a coalition of more than 70 groups representing government, industry, the worker, children and older individuals as well as organizations directly committed to preventing noise-induced hearing loss and providing them with resources in order to reach children under 17, adults in mid-life, and older Americans as a means to provide information about how to prevent fully preventable noise-induced hearing loss with messages in at least 50% of states by 2001.		◆			
Strengthen relationships with constituency groups nationwide to increase awareness of the latest scientific information about drug abuse and addiction prevention and treatment and to provide a channel for feedback about emerging grassroots issues.			◆		
Improve the public's access to health information by expanding the NLM's consumer health information program to ensure that a medical library in every state is working with public libraries and community organizations.			◆		

◆ Target Met	◇ Target Active	◇⟶ Target Not Met and Extended	✖ Target Not Met

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Develop and implement communication campaigns on specific health issues:					
Develop and implement NIH information, education, and outreach programs on specific health issues: Low Vision.	◆				
Expand the outreach of the "Milk Matters" campaign beyond parents and health professionals to focus directly on activities and products that help children and teens recognize the benefit of calcium in building strong bones.		◆			
Generate a minimum of 30 million media impressions through placements in newspapers and magazines nationwide and on national and local television and radio programs, to raise awareness among all Americans of the importance of eating at least 5 servings of fruit and vegetables a day.		◆			
Develop campaign materials about the importance of calcium from milk and other sources for strong bones.				◇	
Implement a stroke awareness campaign.				◇	
Increase the public's awareness of specific health issues and the role of NIH:					
Increase awareness among university presidents, program planners, and policy makers about college drinking and related problems.*			◇→	◇	
Increase awareness among the general public about the achievements of publicly-funded vision research.			◆		
Increase awareness among young people of the importance of calcium in their diet.			◇→	◆	
Increase the number of people who know the symptoms of stroke and rapidly seek treatment.			◆		
Increase the public's understanding of cancer research, advances, and opportunities.			◆		
Increase awareness among the general public that drug addiction is a brain disease.			◆		

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH enhanced its operations to improve the communication of research results.** Prior to FY 2001, NIH successfully implemented a computer system to track inquiries, measure response times, and record customer feedback on NLM services. A toll-free number was also established to improve the public's access to NLM customer service staff, which has generated more than 30,000 calls per year. In addition, NIH restructured the mental health education and information dissemination programs administered by NIMH. Enhanced operations also resulted in substantial increases in the number of on-line health information publications in NIH's Centralized Consumer Health Information area, the usage of NLM's catalog-based databases, and the number of health topics on MEDLINEplus. Finally, an FY 2000 evaluation found that 98% of users surveyed rated NLM's services as

satisfactory or better, and 92% rated the services as good or excellent. These results exceeded the target of 85% of users rating the services as satisfactory.

- **NIH strengthened collaborations with other organizations involved in health communications.** NIH continued to partner with other organizations in FY 2001, meeting its targets to increase public awareness and access to the latest scientific and health information. For example, NLM collaborated with the National Network of Libraries of Medicine to ensure that at least one NLM-supported medical library in every state is working with public libraries and other community organizations to improve the public's access to reliable electronic health information. NIH also met all of its targets in previous years, which included strengthening its relationships with universities, voluntary health associations, and other organizations involved in health communications. For example, in FY 2000 NIH developed a broad coalition for the WISE EARS! communications campaign, which included 78 organizations. NIH has continued to collaborate with professional associations of journalists, science writers, and health communicators to promote coverage of NIH-funded research results.

- **NIH initiated communication campaigns on vision and nutritional health issues.** Prior to FY 2001, NIH successfully developed and implemented campaigns on three health issues involving vision and nutritional health issues: vision loss, the benefits of drinking milk, and the importance of eating at least five servings of fruit and vegetables a day. Implementation strategies included forming strategic alliances with professional organizations that interact with parents and children, and distributing materials to peer leaders and opinion leaders.

- **NIH made significant progress in its efforts to increase the public's awareness of research results.** FY 2001 performance results included: 1) tour of VISION, a traveling exhibit that highlighted the sight-saving results of vision research which reached more than 5.3 million people in 26 metropolitan areas; 2) a stroke education campaign that included radio and TV public service announcements, billboards, a consumer education kit, and an educational video; 3) the expansion of the national 5-A-Day for Better Health campaign; and 4) the development of 160 new cancer information publications. A report on college drinking and related problems originally planned for FY 2001 was delayed until FY 2002 to ensure that new research findings could be included. The report will provide information on the effectiveness of current alcohol prevention strategies and recommendations on future research to improve college drinking prevention programs.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the successful implementation of improved NIH operations, evidence of stronger collaboration with other organizations, and the development and implementation of planned communication campaigns. NIH uses several means to verify performance data and estimate the reach of communications campaigns by analyzing website usage and the number of media requests for interviews, hotline calls, media impressions, and radio and television stations airing campaign messages.

The National Network of Libraries of Medicine (NNLM), covers the entire United States. The mechanisms for this accomplishment range from major multi-year contracts with the eight Regional Medical Libraries (June 2001), subcontracts through these libraries with other institutions in the 4500-member NNLM, and 75 outreach awards from NLM directly to medical libraries and community organizations.

Goal d) Increase awareness of clinical research and support participation in clinical trials.

Increasing public awareness of NIH's need for clinical trial participants is one the agency's greatest communications challenges. NIH researchers conduct clinical trials to determine if new drugs or treatments are safe and effective. Because carefully conducted clinical trials are the fastest and safest way to find treatments that work, NIH needs a steady, diverse, and substantial pool of volunteers including patients and members of the general public. NIH's ability to improve the nation's health care depends on physicians having the opportunity to refer patients to current studies and on patients having the information they need about participating in clinical trials.

In striving to achieve this challenging goal, NIH has focused on increasing clinical trial participation by 1) strengthening collaborations with other organizations, and 2) developing web-based tools and other materials. Because increasing and maintaining awareness regarding clinical trials is difficult, NIH continues to build collaborative relationships with physicians, community groups, and consumer and advocacy groups from across the nation. Web-based tools also serve as important mechanisms for disseminating information to encourage participation in clinical trials. NIH plans to further expand the role of web-based clinical trials tools in the future to improve the development, conduct, and ease of participation in NCI-sponsored clinical trials.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Strengthen collaborations with other organizations to increase clinical trial participation:					
Initiate a broad-based communications and public outreach program to reach physicians, and eventually, community groups and the general public.	◆				
Build and maintain networks of communication and support for clinical research between NIMH and consumer and advocacy organizations and professional groups nationally, regionally, and locally.		◇→	◆		
In partnership with community-based organizations, develop rheumatic disease health education materials and increase awareness of opportunities to participate in clinical studies.				◇	

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Develop web-based tools and other materials to increase clinical trial participation:					
Develop methods and materials to improve communication with minorities and ethnic groups and to encourage them to participate in (NIMH-sponsored) clinical research, thus meeting a critical public health need.		◇→	◆		
Increase visitors to NCI's cancerTrials website and the amount of information about cancer trials to patients, health professionals, the public and the media in all areas including prevention, detection, diagnosis, and treatment.		◆			
Develop simplified and easy-to-understand informed consent forms to help patients better understand a study's treatments and tests and their possible benefits and risks before deciding whether or not to participate.		◆			
Develop web-based clinical trials tools that will improve the development, conduct, and ease of participation in NCI-sponsored clinical trials.			◆		
Improve NCI efforts to increase participation and retain minorities, underserved populations, and the elderly in clinical trials.			◆		
Educate the public about the importance of NIMH-supported clinical research and interest individuals and their families in participating in clinical studies.			◆		
Increase the number of initial contacts about clinical trials with the Patient Recruitment and Public Liaison Office (PRPL).			◆		
Develop messages and materials about participating in clinical studies.					◇

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **NIH successfully launched the Constituency Outreach and Education Program (COEP) to strengthen collaborations with other organizations to increase clinical trial participation.** Although NIH did not fully achieve the FY 2000 target to build and maintain networks of communication and support between NIMH and other organizations, a major five-year communications initiative was successfully launched in FY 2001. The new initiative, called the Constituency Outreach and Education Program (COEP), enlists state organizations in a nationwide partnership to help speed the translation of science into mental health services.

- **NIH developed new web-based tools to increase clinical trial participation.** NIH met all of its FY 2001 targets to develop and maintain web-based tools and other materials designed to educate the public about clinical trials and how to participate in them. Many of the communication activities were directed toward minorities, ethnic groups, and other populations that historically have been underrepresented in clinical trials. For example, NIMH carried out a variety of media activities to increase enrollment in trials, with special attention given to minority audiences. In addition, NCI created the Special Populations Network to address the unequal burden of cancer experienced by certain population groups,

focusing on building strong relationships with research institutions and community-based programs. In FY 2001, NCI extended its outreach efforts to more medical institutions that reach underserved populations including Meharry Medical College (MMC) and the MMC/Vanderbilt-Ingram Cancer Center Partnership. NCI also developed a number of communication tools to increase participation in clinical trials among minority groups and the elderly. Ongoing NCI efforts in this area have raised the proportion of minority participation in treatment clinical trials to nearly 20 percent.

To educate the general public about participating in clinical trials, NIMH developed new web-based and print materials. NCI also developed several web-based informatics "products" to improve the reporting and exchange of clinical trial information, including a clinical data update system and an adverse event reporting system. NCI continued to update its clinical trials database, Physician Data Query (PDQ), which contained more than 1,800 protocols at the end of FY 2001. Also, the Patient Recruitment and Public Liaison Office within the NIH Clinical Center achieved a 37% increase in the number of inquiries it received about participating in clinical trials in FY 2001. Accomplishments in previous years included the development of a simplified informed consent form and a considerable increase in the range of information available on NCI's cancerTrials website and number of website hits.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by evidence of stronger collaborations with other organizations, the development of web-based tools and other materials, and the number of inquiries about NIH-sponsored intramural clinical trials and their availability. NIH uses several means to verify performance data, such as statistical reports on NIH website usage, including downloads of specific NIH tools; the percent of minorities and other underrepresented groups enrolled in NIH-sponsored clinical trials; and the number of telephone inquiries about participating in clinical trials.

PDQ is a database that contains the world's most comprehensive list of cancer clinical trials (more than 1,800 open to patient accrual as of 2001) and is used to report and exchange clinical trials information.

Goal e) Establish a Clinical Trials Database, as required by the FDA Modernization Act.

Many of today's most effective interventions are the direct result of knowledge gained through clinical trials – studies that evaluate the safety and effectiveness of new drugs and other interventions. Therefore, facilitating access to information on clinical trials is an important national goal. In accordance with this goal, the Food and Drug Administration Modernization Act (FDAMA) of 1997 mandated the establishment of a registry of both federally and privately funded clinical trials of experimental treatments for serious or life-threatening diseases submitted under Investigational New Drug (IND) regulations.

In collaboration with other federal agencies, the pharmaceutical industry, and academic and other nonprofit organizations, NIH developed the Clinical Trials Database, a consolidated source of information on clinical trials for drugs for serious or life threatening diseases and conditions. Prior to the development of this database, the NIH homepage provided access to eight separate clinical trials databases: NCI Physician's Data Query (PDQ), AIDS Clinical Trials Information System, Clinical Center Studies, Rare Disease Clinical Trials database, NEI Clinical Trials database, NHLBI Clinical Trials database, NIA Alzheimer's Disease Clinical Trials database, and NIAID Clinical Trials database.

Because improving access to clinical trial information is critical to increasing public and provider awareness, understanding, and willingness to participate in clinical trials, NIH continues to focus on improving and promoting the Clinical Trials Database. For example, NIH is in the process of establishing toll-free telephone access to the database. However, establishing access will be complex and expensive due to uncertainties regarding the demands that could be placed upon the system (i.e., the number of calls), the many possible designs for the system, and the varying levels of service that might be provided. In FY 2001, NIH completed an implementation study to determine the optimal design for the toll-free telephone service, along with operating strategies and associated costs.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Improve and promote the Clinical Trials Database:					
Develop and implement the Clinical Trials Database.	◆				
Expand the Clinical Trials Database to include trials from other federal agencies and the private sector.		◆			
Develop options for implementation of toll-free telephone access to information in the Clinical Trials Database.		◇→	◆		
Complete an implementation study to determine the optimal design and function of a toll-free telephone to facilitate access to the Clinical Trials Database.			◆		
Expand the number of industry-sponsored clinical trials in the database by 250.			◇→	◇	
Expand the number of clinical trials in the database sponsored by other federal agencies by 100.			◆		
Promote the database as a resource for patients, physicians, researchers, community health groups and others.			◆		

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

- **NIH made considerable progress in improving and promoting the Clinical Trials Database.** At the end of FY 2001, the website for the Clinical Trials Database (ClinicalTrials.gov) was receiving about 2 million hits per month and hosting approximately 5,300 visitors each day. NIH successfully completed an implementation study during the year to identify the optimal design and operating characteristics of a telephone service to supplement the database. NIH had previously met its FY 1999 and 2000 targets to develop a prototype system, implement the official Clinical Trials Database, make it available to the public (which occurred on February 29, 2000), and expand the database to include clinical trials sponsored by other federal agencies and the private sector. For FY 2001, the number of industry-sponsored clinical trials was increased by 109**.** FDA guidance on industry-sponsored clinical trials information will be released in FY 2002, which should have an impact on the number of industry-sponsored trials included in the future. It is important to note, however, that the number of trials sponsored by other Federal agencies more than tripled from 104 in FY 2000 to 383 in FY 2001, far exceeding the target. By the end of FY 2001, there was a total of 5,771 trials in the database.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by successful completion of the planned implementation study, the number of clinical trials in the database sponsored by non-NIH organizations, and evidence of

effective promotion of the database. NIH uses several means to verify performance data, including statistical reports analyzing the number of hits on the Clinical Trials Database website (ClinicalTrials.gov).

2.1.2.3 Technology Transfer

The broad purpose of NIH's technology transfer activities is to facilitate and enhance the development of new drugs, other products, and methods of treatment that benefit human health by promoting the efficient transfer to the private sector of new technology resulting from NIH research. Federal legislation empowers NIH to interact directly with industry to expedite the transfer of technological discoveries into commercial products that will benefit the public. In addition to improving public health, technology transfer contributes to the global competitiveness of the nation's businesses and to the nation's economic prosperity.

NIH's technology transfer program is one of the most active in the federal government. NIH patents new drugs, vaccines, devices, and other products developed by its scientists and issues licenses to organizations in the private sector that are interested in the commercial application of these products. To protect the public's research investment, NIH oversees licensee progress and receives royalties from licensees based on product sales. NIH has forged numerous partnerships with industry and other external research organizations, thereby enhancing its capacity to expedite the commercial application of new technologies.

To achieve its full potential in this area, NIH faces a number of challenges: 1) developing effective, well-articulated technology transfer policies and procedures that are understood by NIH scientists, 2) building the organizational structure necessary to facilitate technology transfer for NIH-supported investigators and measure outcomes, and 3) monitoring licensee activities and taking appropriate action against infringers of NIH intellectual property rights. NIH is working with Congress, DHHS, and its research partners to establish and implement rational technology transfer policies that facilitate the patenting and licensing of new technologies and the expansion of cooperative research projects within the NIH intramural research program.

To address these challenges and enhance its technology transfer efforts, NIH established three performance goals:

a) Increase the number of scientists who have received training in technology transfer.

b) Develop a system to identify and measure the health outcomes of technologies licensed by the NIH.

c) Maintain oversight and protection of the public investment in NIH research through increased monitoring of licensee activities.

NIH's efforts to achieve these performance goals include developing new training modules on technology transfer procedures, designing a methodology to measure the health outcomes of NIH-licensed technologies, and developing systems to monitor the progress of NIH licensees and ensure that royalties owed to NIH are paid in a timely manner.

Performance Goal Details - Technology Transfer

Goal a) Increase the number of scientists who have received training in technology transfer.

To maximize NIH's ability to offer cutting-edge technology to the private sector for further development and commercialization, NIH's intramural researchers and technology transfer staff must have access to up-to-date information on the laws, policies, and procedures that govern technology transfer. They must have full knowledge of the federal legislation that empowers NIH to interact directly with industry to expedite the transfer of new technology.

To ensure that NIH scientists (approximately 4,000 research investigators) are able to take advantage of the varied opportunities for translating research results into commercial products, NIH has undertaken two major activities: 1) designing and implementing a web-based training module on technology transfer procedures, and 2) increasing the percent of NIH scientists who have received training in technology transfer. In addition to developing and encouraging participation in the web-based training module, NIH will continue to provide opportunities for its scientists to attend seminars and annual retreats focused on technology transfer policies and related information.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Design and implement a web-based training module on technology transfer procedures:					
Contractor development of a web-based training module.	◇→	◆			
Implement training module.		◇→	◆		
Increase the percent of NIH scientists who have received training in technology transfer:					
Contact 20% of NIH scientific staff.		◇→	◆		
Seek to have 15% of scientists complete the training module and/or attend technology transfer seminars.			◆		
200 scientists complete the web-based training module.				◇	
1,000 scientists complete the web-based training module.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH successfully implemented the web-based training module on technology transfer procedures.** Although NIH encountered software development delays, the web-based training module was activated successfully in the first month of FY 2001 (October 2000).

- **Over one-half of NIH scientists have received training in technology transfer.** Approximately 2,450 of the 4,000 NIH scientists (63%) attended the training seminars. As a result, NIH surpassed its training targets for FY 2001, FY 2002, and FY 2003.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the number and percent of NIH scientists who attended seminars/retreats focused on technology transfer. NIH uses participation information collected from seminar attendance sheets to verify these performance data.

Goal b) Develop a system to identify and measure the health outcomes of technologies licensed by NIH.

Effectively measuring the public health outcomes that result from technologies licensed by NIH is challenging and complex. Traditionally, efforts to measure the impact of technology transfer activities have focused on countable outputs, such as the number of licenses issued. However, this approach does not provide very useful information and may, in fact, distort the importance of NIH's technology transfer achievements.

To address this challenge, NIH established in FY 2001 a new goal to develop a system for measuring key outcomes of interest to managers and policymakers. NIH's strategy for developing a better measurement system focuses on designing and testing a methodology for measuring the outcomes of new drugs, vaccines, and devices. The first step is to establish an internal working group that will identify potential data sources and outcome measures. At this time, potential outcome measures include: dosages prescribed or used, reduction in mortality/morbidity, reduction in number of sick days used, and extension of life. After specific data sources and outcome measures have been selected, NIH will conduct a limited pilot-test of the proposed methodology and apply the final methodology to a sample of licensed technologies that have been incorporated in commercially available products.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Design and test a methodology for measuring outcomes of new drugs, vaccines, and devices.					
Establish a working group in the Office of Technology Transfer and obtain recommendations on potential outcome measures and sources for obtaining reliable data for those measurements on therapeutic drugs, vaccines, and devices.			◇→	◇	
Develop two case studies to test the proposed methodology.				◇	
Finalize the approach and apply the methodology to 10% of all exclusively licensed technologies that are part of commercially available products.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH established a working group to develop health outcomes measures with recommendations to follow.** NIH established a working group to develop health outcomes measures. However, due to a change in leadership at the OTT, the full implementation of this goal was delayed. NIH staff have completed background research and developed a potential study design, including a list of data sources that will be presented to the Working Group for consideration. Recommendations on reliable data sources and potential outcome measures for therapeutic drugs, vaccines, and devices will be developed in FY 2002.

Verification/Validation of Performance Measures and Data Issues

Performance will be measured by completion of the recommendations on potential outcome measures and data sources, by completion of the pilot-test, and by application of the methodology to a sample of licensed technologies. Performance data will be verified through records maintained by the NIH Office of Technology Transfer.

Goal c) Maintain oversight and protection of the public investment in NIH research through increased monitoring of licensee activities.

Whereas the transfer of technology from research to commercialization is an important concern, it is equally important to ensure that licenses of technologies to commercial entities are implemented properly and that the correct amount of royalties is paid to the government. To minimize the risks associated with noncompliance with licensing agreements, NIH established a new goal in FY 2001 to implement a new monitoring strategy for licensed technologies.

The monitoring effort consists of three major activities: 1) designing and implementing a system for monitoring the progress of NIH licensees, 2) ensuring that royalties owed to NIH are made in a timely and appropriate manner, and 3) pursuing litigation against entities who are infringing on NIH intellectual property rights.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Design and implement a system for monitoring the progress of NIH licensees:					
Recruit and select personnel to establish a special license-monitoring unit to provide oversight of licensee progress in developing and commercializing technologies licensed from NIH.			◇→	◇	
Implement a data system that includes all license monitoring milestones and benchmarks for all exclusive licenses.				◇	
Ensure that royalties owed to NIH are made in a timely and appropriate manner:					
When indicators show that sales and royalty information may be incorrect, conduct audits of up to 3 licensees during the year.			◆		
Reduce the number of delinquent payments over 180 days by 50% from the number in place at the end of FY 2000.			◆		
Reduce the number of terminated licensees with outstanding royalty amounts owed by 10% from the number at the end of FY 2000.			◆		
Reduce delinquencies over 180 days and bring that number to zero by the end of FY 2002, except for cases that are being actively negotiated due to the affect on public health.				◇	
Ensure that all delinquent payments associated with terminated licenses will be submitted to the NIH Debt Collection Officer within 120 days of termination.				◇	
Perform audits on up to 3 licensees during the year, if warranted.				◇	
Pursue litigation against entities who are infringing on NIH intellectual property rights:					
Develop and implement a process to refer infringers of NIH intellectual property rights to the Department of Justice with recommendations for bringing a federal lawsuit against such entities.			◆		

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

- **Lack of qualified candidates slows recruitment effort.** A recruitment effort was executed, but qualified candidates were not found. These positions will be re-announced in FY 2002.

- **NIH reduced delinquent payments considerably.** NIH took numerous steps in FY 2001 to ensure that royalties owed to NIH were paid. Audits were conducted on 5 licenses, which exceeded the target (3 were planned). Revised procedures enabled NIH to reduce the number of delinquent payments (over180 days late) from 78 in FY 2000 to 35 in FY 2001. This decrease represents a 55% reduction in the number of delinquent payments owed, which is 5% more than targeted. Additionally, NIH improvements led to the decline in the number of terminated licenses with outstanding balances from 21 in FY 2000 to only 12 in FY 2001.

- **NIH implemented a new litigation process against infringers.** A process for referring infringers of NIH intellectual property rights to the Department of Justice has been developed and implemented. NIH has initiated three cases; one was settled before being filed with the court and two are pending.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the number of licensees audited, by the number and percent reduction in delinquent royalty payments and terminated licenses, and by the implementation of a process for pursuing litigation against those who infringe on NIH intellectual property rights. NIH uses several means to verify performance data, including records maintained by the NIH Office of Technology Transfer regarding licensee audits, delinquent payments, terminated licenses with outstanding balances, and court actions.

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2.1.2.4 Research Leadership and Administration

To expedite progress in medicine and health care, NIH sets research priorities, encourages scientific innovation, employs an effective and fair process to determine which scientific projects and scientists receive funding, and efficiently uses the resources available to support medical research. NIH views its leadership in these realms as essential to maintaining proper stewardship of the nation's medical research enterprise.

All of the NIH ICs are actively involved in research leadership and administration, which requires effective coordination of the following three functions:

Priority setting – implementing decision-making mechanisms and policies that ensure NIH research is responsive to emerging health needs, scientific opportunities, and new technologies.

Grants administration and peer review – maintaining effective and efficient grants administration and a high quality of peer review to ensure the most meritorious research projects are considered for funding.

Agency management and administrative support – ensuring that management and administrative functions necessary to support the agency's mission are carried out effectively and efficiently.

To enhance its research leadership and administration capabilities, NIH established performance goals for each of these functions.

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Priority Setting

Establishing priorities to decide how NIH should allocate its funding is a complex process involving input from a broad range of stakeholders and decision-makers at various levels within the NIH and DHHS. Congress ultimately determines the overall NIH budget and individual IC budgets, with the President's agreement, but NIH plays a major role in the decision-making process. Its priority setting policies and procedures are designed to ensure that NIH research is responsive to emerging public health needs, scientific opportunities, and new technologies.

The expert knowledge and recommendations provided by patient advocacy groups, scientists, health care providers, and the general public influence NIH research policies, IC strategic plans, new program announcements encouraging grant applications in specific areas, and the decisions that NIH ultimately makes about resource allocation for biomedical research. These stakeholders' long-standing interest in priority setting at the NIH was a factor in the FY 1998 Congressional mandate for the Institute of Medicine (IOM) to conduct a comprehensive study of the policies and processes used by the NIH to determine funding allocations for biomedical research. NIH has been engaged in, and effectively responded to, the IOM recommendations.

Many considerations influence NIH budget planning and decision-making, including: 1) an obligation to respond to public health needs; 2) a commitment to support research of the highest scientific caliber; 3) a responsibility to seize the scientific opportunities that offer the best prospects for new knowledge and better health; 4) a need to maintain a diverse portfolio that supports work in many scientific disciplines and on a wide range of diseases; and 5) an obligation to maintain the nation's strong scientific infrastructure, including a high quality workforce and excellent research facilities.

NIH currently has one performance goal for priority setting:

a) Ensure that NIH-supported research reflects the changing nature of scientific opportunities and public health needs.

The activities that NIH is undertaking to achieve this goal, which are reflected in the annual performance target, include sponsoring IC workshops and panels to identify scientific opportunities and health needs, and incorporating the participants' recommendations into future requests for research applications.

Performance Goal Details - Priority Setting

Goal a) Ensure that NIH-supported research reflects the changing nature of scientific opportunities and public health needs.

Establishing and continuously updating research priorities is essential to ensuring scientific progress, meeting national needs, and efficiently using available resources. Setting priorities is a complex process involving consideration of many factors, including determining which areas of science are ripe for pursuit and how research can best be harnessed to meet public health needs. Many considerations influence the planning and spending of budgets, and NIH solicits opinions about them from the extramural scientific community, patient advocacy groups, health care providers, Congress, the Administration, and NIH staff. These opinions are gathered through various means, as appropriate to the decision-making process. For example, peer review panels composed of accomplished investigators are regularly convened by NIH to evaluate grant applications for scientific merit; national advisory councils, with members representing the public, medical, and scientific communities, are often asked to review specific policies; external advisory groups are used when needed to assess NIH-wide activities and to recommend programmatic directions based on changes in the science and public health needs; and representatives of patient groups and other health advocacy organizations, DHHS, OMB, other federal agencies, and the Congress are encouraged to participate in workshops and provide input on a variety of issues of common concern.

Annual Performance Target	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Sponsor Institute and Center workshops and panels that assess scientific progress and opportunities and identify emerging public health needs. Incorporate findings and recommendations from these workshops and panels into updated proposal submission requests for Institute and Center research programs.	◆	◆	◆		

Note: This goal is part of the normal research grant selection process and will not be continued past FY 2001.

◆ Target Met	◇ Target Active	◇⟶ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **NIH continues to sponsor planning activities to identify emerging public health needs and identify new programmatic initiatives.** The factors that influence the planning and spending of the NIH budget are complex, and input from a broad range of individuals and organizations is sought to inform the decision making process. Convening workshops, conferences, panels, and other meetings with representatives from the public, medical, and scientific communities is an important means for gathering opinions, assessing NIH-wide activities, and recommending programmatic directions based on changes in science and

public health needs. In FY 1999, FY 2000, and FY 2001, NIH Institutes and Centers used outside experts at workshops, panels and other meetings to assess scientific progress and opportunities and collect input for the priority setting process.

Verification/Validation of Performance Measures and Data Issues

This goal primarily involves identification of the scientific/public health areas for which workshops were held, the recommendations made, and the changes in existing or implementation of new research program initiatives. Performance assessment will be based on evidence including: (1) workshops, panels, and other meetings held to solicit public input into NIH activities and (2) issuance of Requests for Applications (RFA), Program Announcements (PA), and Requests for Proposals (RFPs) that encourage research in areas of identified need.

Listings of workshops and other meetings convened by the Institutes and Centers are routinely maintained and a matter of public record. Likewise, agendas and reports or summaries of these meetings, lists of program announcements (PA), requests for applications (RFA), and requests for proposals (RFP) issued by the Institutes and Centers are publicly available. The content of PAs, RFAs, and RFPs provides a cross-check for consistency with the recommendations from the workshops or other forums.

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Grants Administration and Peer Review

Approximately 80 percent of NIH's budget supports research conducted in universities, medical centers, and other institutions around the country, with most of the research funding provided through competitive research grants. Therefore, it is essential for NIH to maintain effective and efficient processes for reviewing, selecting, and administering extramural research grants.

To ensure that the most meritorious research projects are considered for funding, NIH employs a peer review process in which prominent scientists from around the country evaluate each request for support, and through this process, provide advice to NIH staff in the selection process. NIH strives to ensure that the peer review process is fair, reflective of state-of-the-art knowledge of the science being reviewed, and able to accommodate the many applications for research support and training that NIH receives. After NIH awards funds to a particular project, administrators in the sponsoring IC provide oversight to ensure that the research is carried out appropriately.

In addition to ensuring that the highest quality research is selected for support, NIH is committed to providing support to investigators in a timely fashion so that their research can proceed efficiently. The expenditure of the nation's financial resources for the conduct of research also demands appropriate oversight, which requires effective grants administration, prompt customer service, and efficient communication and reporting processes. Related challenges include strengthening NIH's capacity to receive and transmit grant information via the Internet using electronic Research Administration (eRA) technology and improving the Edison electronic invention reporting system.

To address these challenges and enhance the effectiveness of grants administration and peer review activities, NIH established five performance goals:

a) Improve electronic Research Administration (eRA) technology by developing capability for end-to-end electronic research administration by 2004.

b) Ensure proper stewardship of public funding for research.

c) Ensure that the NIH peer review process keeps pace with current advances in research and that the expertise of the peer reviewers is appropriate for the needs of modern science.

d) Develop innovative business practices to facilitate government/public interactions.

e) Improve grantee reporting of inventions developed with federal funds.

NIH's efforts to achieve these performance goals include developing new modules for the NIH Commons system to enable NIH to receive grant applications and progress reports electronically, simplifying the administrative processes required of grantees, enhancing the design of the Edison invention reporting system, improving the organization of the peer review system, and increasing educational outreach to improve institutional compliance with NIH requirements.

Performance Goal Details - Grants Administration and Peer Review

Goal a) Improve electronic Research Administration (eRA) technology by developing capability for end-to-end electronic research administration by 2004.

NIH is implementing a software development and staged interface deployment process to enhance the electronic exchange of essential information between NIH and research institutions. Central to these improvements is the concept of the "NIH Commons," a web-based information interface enabling NIH and the grantee community to conduct their business using electronic Research Administration (eRA) technology. The NIH Commons is a relational client/server database, designed to be compatible with the Federal Commons system. The NIH Commons includes modules designed to greatly facilitate the preparation of grant applications, processing of applications by NIH staff, and management of awards by grantee institutions and NIH staff. NIH has also taken a leadership position in the development of the Federal Commons system, an interagency effort designed to expedite the sharing of information among government agencies and departments, which will ensure that the NIH Commons incorporates government-wide eRA standards.

NIH's major activities in this area include: 1) designing and testing several new modules within the NIH Commons system; 2) testing and implementing the electronic receipt of grantee progress reports; and 3) testing and implementing the electronic receipt of competing R01 applications. The following modules of the NIH Commons are in various stages of development/deployment:

- The Grant Applications/Awards Status module allows investigators and grant administrative officials to obtain information about the current status of their pending grant applications and awards electronically.
- The Electronic Notice of Grant Award (NGA) module enables NIH grant and cooperative agreement recipients to receive the official notification of award electronically.
- The Streamlined Noncompeting Award Process (SNAP) modules enable principal investigators and administrative officials at grantee institutions to submit electronically the scientific and administrative information necessary for continuation of a multi-year grant award. Using SNAP, the annual progress report and other information required for a noncompeting continuation (type 5) application can be submitted electronically, replacing the hard copy Form PHS 2590. There are two SNAP modules: e-SNAP handles the simpler awards and CNAP handles the more complex awards.
- The Accounts Administration (Admin) module permits the addition, deletion, and modification of user accounts and the viewing and updating of professional and institutional profiles electronically.
- The Trainee Activities System (X-Train) module allows grant administrative officials to record and obtain information about their trainee appointments electronically.

- The Fellowships module will enable fellowship applicants and administrative officials to submit an electronic application for an individual PHS National Research Service Award (NRSA), replacing the hard copy Form 416-1.
- The Competing Grant Award Process (CGAP) module will enable principal investigators and grant administrative officials to submit an electronic application for an R01 or other type of competing grant award, replacing the hard copy Form PHS 398.

The 65 research universities and non-profit research centers participating in the Federal Demonstration Partnership (FDP) are being used to pilot-test the new NIH Commons modules.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Design and test new modules within the web-based NIH Commons system:					
Design and test new systems.	◆				
Streamline post-award reporting while continuing to ensure appropriate oversight and enhancement of recipients' compliance with reporting and accountability requirements.	◆				
Full deployment of key eRA business process modules.		◆			
Release NIH Commons modules in the new architecture.				◇	
Test and implement electronic receipt of grantee progress reports:					
Implement electronic progress reporting with all 65 newly on-line institutions participating in the Federal Demonstration Partnership.		◇→	→	◇	
Begin pilot testing of progress reporting for multi-project mechanisms.		◇→	→	◇	
Test and implement electronic receipt of competing R01 applications:					
Scan all incoming competing R01 applications in preparation for pilot testing receipt of R01 applications in 2003.				◇	
Pilot-test electronic receipt of simple (non-clinical, non-human) competing R01 applications.					◇

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

- **NIH designed and tested new modules in the NIH Commons system.** Prior to FY 2001, NIH made significant progress with respect to several modules. During a small pilot test of the e-SNAP module, NIH received 22 continuing applications electronically. Subsequently, NIH expanded the pilot to involve 10 grantee institutions. NIH's web-based CRISP system provides public access to updated scientific abstracts collected through e-SNAP.

NIH also conducted a small pilot test of the X-TRAIN module involving 15 institutions, which involved the electronic transmission of trainee appointment information. The NGA module was fully deployed in FY 2000, and NIH made nearly 70% of all notifications of award electronically. NIH has also worked with other agencies to develop standard data dictionaries for the Federal Commons system.

- **Pilot tests revealed the need for improved progress reporting technology.** During pilot testing, NIH found the technology used in the prototype for electronic receipt of grantee progress reports to be inadequate. As a consequence, both FY 2000 targets were reassessed and extended to FY 2002. In FY 2001, NIH developed the infrastructure needed to support a more effective progress reporting technology. NIH also completed the business process reengineering necessary for development of an electronic progress reporting system. Pilot deployment is scheduled for FY 2002.

- **Testing and implementation of electronic receipt of competing R01 applications is on schedule for FY 2002 and 2003.** Progress will be reported in February 2003 and February 2004, respectively.

Verification/Validation of Performance Measures and Data Issues

Performance will be measured by the extent to which information can be submitted to NIH through the Federal Commons system and by the number of FDP institutions registered, R01 applications scanned, and progress reports and R01 applications received each year. Performance data will be verified through eRA status reports posted on the OER website.

Goal b) Ensure proper stewardship of public funding for research.

With the receipt of NIH grant awards or other types of public funding for research, principal investigators and grantee institutions accept the responsibility to conduct scientific studies ethically and honestly, and to provide proper stewardship of NIH funds. Because of the nature of the assistance relationship, which is predicated largely upon trust between the sponsor (NIH) and the recipient (grantee institution), the need for effective internal and external compliance programs is essential. To minimize the risks associated with noncompliance, NIH established a new goal in FY 2001 to ensure proper stewardship of public funding for research. This cross-cutting goal involves NIH Institutes and Centers working in partnership with grantee institutions and national professional organizations to improve institutional compliance with NIH requirements.

NIH's strategy for enhancing compliance is to develop a proactive grants compliance program. The program currently focuses on two major activities: 1) enhancing administrative oversight by creating a new organizational component within NIH with the capacity to perform at least 10 compliance site visits a year, and 2) increasing educational outreach by providing web-based information and tools to help grantees understand their stewardship role and improve their institutional compliance programs.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Enhance NIH's administrative oversight of sponsored research:					
Create an organizational component within NIH with FTEs devoted expressly to compliance-related activities.			◆		
Perform a minimum of 10 compliance site visits.			✖		
Increase educational outreach to improve institutional compliance with NIH requirements:					
Publish a compendium of observations and examples of compliance in action in the conduct and administration of sponsored programs at NIH's recipient institutions.				◇	
Provide Internet-accessible resource information and/or tools for implementing institutional compliance programs.					◇

◆ Target Met | ◇ Target Active | ◇⟶ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **Administrative oversight enhancements were completed.** NIH established the Division of Grants Compliance and Oversight in August 2001 with three full-time-equivalents (FTEs) assigned to compliance-related activities. However, it was also deemed unnecessary to perform a minimum of 10 compliance site visits. Based on the compendium of findings and

recommendations that have resulted from completed compliance site visits, NIH determined that focusing on different types of institutions (e.g., HBCU and Research Institute) for site visiting would be more productive and efficient than conducting 10 site visits. As a result, NIH completed eight proactive compliance site visits in FY 2001.

- **NIH is increasing educational outreach to improve institutional compliance.** No performance has been reported to date. Reporting will begin in February 2003.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by completion of the organizational chart and other paperwork required to establish the compliance unit and by the number of compliance site visits conducted during the year. Performance data can be verified through site visit records maintained by the NIH Office of Personnel and postings on the Office of Extramural Research (OER) website of the organizational chart.

Goal c) Ensure that the NIH peer review process keeps pace with current advances in research and that the expertise of peer reviewers is appropriate for the needs of modern science.

NIH's peer review system is recognized as the cornerstone of the NIH extramural program because it is the principal mechanism by which the Institutes and Centers identify high quality research that is worthy of funding. Established over 50 years ago, the system has been outstandingly successful and in fact, may be the most important single reason for the remarkable success of our federally funded biomedical research enterprise. The NIH Center for Scientific Review (CSR) manages the peer review process for approximately three-fourths of the 40,000 grant applications submitted to NIH each year. Grant applications are initially reviewed for scientific and technical merit by peer review groups (study sections), which are composed primarily of non-government research scientists.

For decades, the individual study section served as the functional unit of review. To enhance the review process, NIH recently adopted the Integrated Review Group (IRG), a cluster of scientifically related study sections, as the functional unit of review. The IRG is an administrative unit including a number of study sections encompassing a broad scientific domain (analogous to an academic department). Currently in CSR there are 150 standing study sections clustered within 20 IRGs. To ensure that the NIH peer review process can adequately address the rapid progress in biomedicine and accelerating rate of change, NIH has undertaken two major activities: 1) improving the organization of the peer review system to keep pace with advances in science; and 2) enhancing study section operations by forming more external IRG Advisory Groups.

A comprehensive examination of the organization and function of the CSR peer review system is being conducted by the Panel on Scientific Boundaries for Review (PSBR), a group established by the CSR Advisory Committee in 1998. It consists of highly recognized experts in the biomedical and behavioral sciences. The Panel's Phase 1 report, completed on schedule in FY 2000, identified a current need for 24 IRGs, 17 of which would require the design of new study sections. During Phase 2, an internal Steering Committee will be established for each of these 17 IRGs to identify its key scientific areas and to recommend experts outside NIH to serve on a Study Section Boundary (SSB) Team, which will be charged with designing the IRG's study sections.

In addition to this broad reorganization effort, NIH has been establishing external IRG Working Groups who meet approximately once every five years to assess whether the current study sections within each IRG have the necessary scope and depth of expertise to review applications in their area of science. To date, such IRG Advisory Groups have been designated for 8 of the 20 current IRGs. As part of its effort to enhance study section operations, NIH is in the process of increasing the number of IRG Advisory Groups. NIH's focus on these two major activities ensures that the peer review system will be able to accommodate the review of more complex, diverse, and multidisciplinary research proposals.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Improve the organization of the peer review system to keep pace with advances in science:					
Conduct various assessments of the functions and organization of NIH study sections.	◆				
Complete Phase 1 of the Panel on Scientific Boundaries for Review (PSBR) and develop an implementation plan for Phase 2.		◆			
Create 4 Steering Committees and their respective Study Section Boundary (SSB) Teams.			◆		
Increase the number of Steering Committees and SSB Teams to 10.				◇	
Implement modifications to 4 Integrated Review Groups (IRGs) based on recommendations of the PSBR, the Steering Committees and SSB Teams.					◇
Complete formation of all Steering Committees and SSB Teams. [1]					◇
Enhance study section operations by forming more external IRG Advisory Groups:					
Double the number of external IRG Advisory Groups from 3 to 6.		◆			
Increase the number of external IRG Advisory Groups to 14.			◆		
Complete the formation of all external IRG Advisory Groups.[2]				◇	

[1]The Phase 1 report of the PSBR found that there is a current need for 17 IRG Steering Committees and SSB Teams.
[2]The total number of IRG Working Groups needed has not yet been determined.

◆ Target Met	◇ Target Active	◇⟶ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **Peer review system improvements are on schedule to keep pace with advances in science.** NIH created seven Steering Committees and their respective Study Section Boundary Teams, exceeding its target of 4, in FY 2001. In prior years, NIH completed the final Phase 1 PSBR report and initiation of the Phase 2 implementation plan. Integration of the neurosciences and AIDS study sections, and the behavioral and social science study sections were also completed.

- **Enhancements of study section operations are ahead of schedule.** The FY 2000 target to double the number of external IRG Advisory Groups from 3 to 6 was significantly exceeded with 10 Advisory Groups formed during the year. Seeking to build on this success, NIH revised the FY 2001 target to 14. By forming nine additional groups, NIH's actual performance exceeded the revised FY 2001 target considerably.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the number of Steering Committees, SSB Teams, and external IRG Advisory Groups in operation at the end of each fiscal year, and by completion of modifications to specific IRGs and their study sections. Performance data can be verified through postings on the CSR website describing progress in implementing Phase 2 and dissemination for public comment of the proposed IRG and study section modifications.

Goal d) Develop innovative business practices to facilitate government/public interactions.

NIH is committed to increasing the efficiency of its policies and procedures to improve customer service to grantees without diminishing its ability to provide appropriate oversight of its research portfolio. To help simplify grants administration processes, the NIH Office of Extramural Research (OER) has identified two priority areas: 1) shortening the time between submitting a grant application and receiving research funds; and 2) simplifying the administrative processes required of grantees.

Reducing the grant award cycle will allow the highest quality research to begin sooner and permit already productive research programs to continue uninterrupted. Even in instances where funding cannot begin earlier (e.g., funding a competing continuation application must await the end of the previous noncompeting segment), earlier *notification* of pending awards will provide more stability to the research enterprise. A major success in expediting the awards process has been the recent establishment of procedures to expedite Institute Advisory Councils' concurrence with study section recommendations – a procedure called "expedited en bloc concurrence." In essence, Council concurrence for the most meritorious applications (generally defined as those with technical merit ratings in the top 15% across NIH) can now be obtained prior to the next scheduled Council meeting, permitting more timely awards.

To simplify the administrative processes required of grantees, NIH has responded to suggestions from the extramural research community to identify ways to reduce the number of steps and information required for a noncompeting continuation of a multi-year grant award. For example, NIH will begin a small pilot test to provide more flexibility to grantee institutions using the streamlined noncompeting award process (SNAP), allowing the required information to be submitted directly by each grant's principal investigator instead of the institution's business office.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Shorten the time between submitting a grant application and receiving research funds:					
Identify approaches to expedite the processing and award of grant applications.	◆				
Expedite the processing of the most meritorious grant applications by extending to all NIH Institutes the use of expedited en bloc Council review procedures.		◆			
Further facilitate expediting the processing of the most meritorious grant applications by reducing the receipt-to-award cycle from 9-10 months to 6-7 months.			◆		
Simplify the administrative processes required of grantees:					
Pilot-test ways to further simplify NIH's Streamlined Noncompeting Award Process (SNAP).				◇	
Evaluate the results of the simplified SNAP pilots and make recommendations.					◇

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

- **Significant progress has been made in shortening the application-to-award cycle.** NIH successfully shortened the time between grant submission and receipt of funds or notification by establishing the process of expedited en bloc Council concurrence. The 13 Institutes employing the process expedited 50-75% of Type 1 (new) awards and provided early notification for Type 2 (competing continuation) awards, thus making or providing notification of awards to the most meritorious grant applications in approximately 6-8 months from application receipt. Two additional Institutes expect to begin using the expedited process within the next year. Importantly, NIH has identified a number of factors beyond NIH control that limit the ability to reduce time to award across NIH. These factors are related to applicants' abilities to accept an award and the annual Federal budget process.

- **Action to simplify the administrative processes required of grantees will be completed in FY 2002 and 2003.** Progress will be reported in February 2003 and February 2004, respectively.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the percent of Type 1 awards expedited, the early notification of Type 2 awards, and the number of months it took the most meritorious grant applicants to receive funding or a notice of award. Performance data can be verified through comparisons of grant application data in the IMPAC database system with accounting data maintained by the NIH Office of Financial Management.

By employing expedited en bloc Council concurrence, NIH has found that certain factors limit the expediting of awards: (1) applicants may decline the offer of an early Type 1 award to ensure that additional staff are hired and in place, and appropriate collaborations are fully established; (2) Type 2 applications are tied to an existing end date, so that the start date for making the Type 2 award is fixed; and (3) the Federal budget process, including the practice of using Continuing Resolutions, prohibits the NIH from using expedited procedures for a least one of the three Council rounds (October). In some years, the budget process may also affect the January round.

One-third of the Institutes use their websites to inform the community of the percentile they will assure funding for research project grants. Consequently, as soon as applicants receive their scores from peer review (approximately 4-5 months after application submission), they know they will be funded if they are within that percentile payline. For these Institutes, this percentile payline is usually above the 20th percentile, thus successfully extending the definition of "most meritorious awards" past the originally anticipated 15th percentile.

Goal e) Improve grantee reporting of inventions developed with federal funds.

The Bayh-Dole Act was enacted in 1980 to ensure the transfer of technology from federally funded extramural research facilities to the commercial/public sector. The Act stipulates that all grantees must report on inventions, patents, and licenses resulting from federally funded research. To support this requirement, NIH has developed a web-based system called "Edison," which is designed to receive, store, sort, and provide reports on inventions, patents, licensing, and invention utilization. Edison is the first secure interactive website developed as part of the NIH electronic Research Administration (eRA) system.

A recent analysis of trends in NIH award and invention reporting found that more than 90% of grantee/contractor institutions that do routine invention reporting use Edison to meet their patent and invention reporting needs. Another study found that the use of Edison has significantly reduced the number of cycles of paper correspondence typically involved in patent and invention reporting from 15 to 3, dramatically reducing reporting time and effort. In addition, Edison makes more information available in a usable format for grants administrators.

To further improve grantee reporting of inventions, the NIH Office of Extramural Research (OER) is focusing on two major activities: 1) fully establishing the web-based Edison invention reporting system, and 2) improving the implementation and design of the Edison system. In addition to demonstrating the use of Edison by all grantee institutions registered to do electronic commerce with NIH, its use will also be expanded to other government agencies. A variety of improvements to the system will also be made, including improving the quality of the historical data in the system, developing a best practices document for constituents based on information gathered during compliance site visits, and integrating Edison into the Federal Commons system. The redesigned Edison system will be deployed to 350 grantee/contractor organizations in FY 2003.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Fully establish the web-based Edison invention reporting system:					
Enhance recipient compliance with reporting and accountability requirements.	◆				
Fully establish the Edison system for use by all grantee institutions, and expand its use to other government agencies.		◆			
Improve the implementation and design of the Edison system:					
Identify ways to improve the quality of historical invention reporting data.			◆		
Further educate constituents of their invention reporting obligations.			◆		
Integrate Edison into the Federal Commons (a governmental grants and contracts administration system).				◇	
Deploy a redesigned Edison system to 350 grantee/contractor organizations.					◇

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **The web-based Edison invention reporting system has been established and is producing results.** The FY 1999 and 2000 targets to fully establish the Edison system were both met and as a result, at the end of FY 1999, 189 grantee institutions were using Edison, a 40% increase since FY 1998. Also, two additional federal agencies signed Memoranda of Understanding indicating they would begin using Edison to meet their patent and invention reporting requirements. By the end of FY 2000, the Edison system was capable of being used by all grantee institutions registered to do electronic commerce with NIH. Altogether, 273 institutions and 12 government agencies were registered to use Edison, which represented a 44% increase in the number of institutions and a 20% increase in the number of agencies since FY 1999.

- **The NIH has significantly improved the implementation of the Edison system.** In FY 2001, to improve the quality of historical invention reporting data and following discussions with grantees on ways to improve the implementation of the Edison system, NIH increased the number of full-time staff dedicated to the thorough analysis of historical records by adding two contractors to the staff. As part of their duties, these staff interact directly with NIH grantee organizations to increase awareness of historical invention records and reporting obligations, to reconcile historical records, and to resolve any other outstanding data issues. In addition, NIH staff responsible for invention reporting participated in all proactive compliance site visits in FY 2001. At the site visits, staff interviewed grantee organization intellectual property professionals regarding policy and invention reporting procedures. Such interactions offered a means by which NIH staff could provide advice for improving

reporting compliance practices. The interactions also provided material for an on-line compendium of observations, contributing to a set of best practices to which the grantee community may refer as they seek to improve invention reporting compliance. Finally, presentations at national meetings of academic technology transfer and grants administration professionals allowed NIH to continue to reinforce the importance of statutory invention reporting to its constituency. Now NIH will focus its attention on the targets intended to address improvements to the design of the Edison system, first integrating it into the Federal Commons and subsequently deploying a redesigned system.

Verification/Validation of Performance Measures

Performance data for the target on educating constituents can be verified on the NIH grants compliance website at http://grants.nih.gov/grants/compliance. Schedule and findings for NIH proactive compliance site visits are discussed

Performance data for the target on improvement of quality of historical invention reporting data can be retrieved from the Edison database.

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Agency Management and Administrative Support

To maintain its world-class stature in research, NIH must maintain effective internal management systems and provide strong administrative support to the research community. NIH provides all of the ICs with centralized management systems and support services to enable them to pursue their research goals unimpeded by administrative obstacles and inefficiencies.

Centrally provided support services include: 1) advising the NIH Director and staff on all phases of NIH-wide management and administrative activities, 2) providing leadership and direction to all aspects of management, and 3) overseeing administrative functions (e.g., budget and financial management, personnel management, management policy, management assessment, program integrity, contract procurement and logistics management, engineering services, safety, space and facilities management, support services, and security operations).

In addition to these ongoing responsibilities, current challenges in the management and administrative support area include ensuring that NIH's decisions regarding information technology lead to sound investments that support the overall NIH mission, and improving the efficiency and effectiveness of all NIH procurement and contracting activities.

To address these challenges and provide improved management and administrative support, NIH established six performance goals:

a) Implement the recommendations of the Arthur Andersen, Inc. study of administrative practices and costs at NIH.

b) Improve the efficiency of the small acquisition process by continuing to expand the Purchase Card Program.

c) Expand the use of Performance Based Contracting (PBC).

d) Identify and pilot new approaches to providing human resource services which increase manager satisfaction with personnel system flexibility and ease of use.

e) Recruit and retain highly qualified extramural investigators to biomedical/ behavioral research through the use of student loan repayment programs.

f) Implement government-wide initiative on delayering management levels and streamlining organization.

NIH's efforts to achieve these performance goals involve increasing the dollar volume of purchase card orders, increasing the amount of NIH contracting dollars that are allocated to performance-based contracts, and delegating human resource authorities to the ICs.

Performance Goal Details – Agency Management and Administrative Support

Goal a) Implement the recommendations of the Arthur Andersen, Inc. study of administrative practices and costs at NIH.

After a seven-month review, Arthur Andersen, Inc. made 80 recommendations aimed at enhancing the efficiency and effectiveness of NIH's business operations. These recommendations included such activities as: establishing a Center for Information Technology, hiring a Chief Information Officer, decentralizing acquisitions, elevating the Chief Financial Officer position to the Deputy Director of Management level, and undertaking a major technology transfer education and orientation program.

The NIH Director and the IC Directors initially reviewed the 80 recommendations, after which NIH established an Arthur Andersen Implementation Oversight Committee to independently determine which recommendations were appropriate for implementation. In FY 1999, NIH accepted 95 percent (76 of 80) of the recommendations and began to implement them. By the end of FY 2001, NIH fully met its goal of complete implementation of the Arthur Andersen recommendations.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Implement the recommendations of the Arthur Andersen study in a timely manner:					
Complete NIH Director and IC Directors review and decision-making for all recommendations.	◆				
Implement recommendations related to the Chief Information Officer and the Chief Financial Officer.	◆				
Complete the implementation of all recommendations as decided upon by the NIH Director and IC Directors.		◇→	◆		

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH has completed implementation of the Arthur Andersen study recommendations.** Since beginning the implementation process, NIH has hired a Chief Information Officer and elevated the Chief Financial Officer position to the Deputy Director of Management level. NIH completed its implementation of the 76 approved recommendations during FY 2001.

Verification/Validation of Performance Measures and Data Issues

The Division of Quality Management (DQM), NIH, and the Deputy Director for Management (DDM), NIH monitored the implementation of the Andersen, Inc. recommendations with an emphasis on the actions required to deal with priority issues. DQM issued quarterly requests for updates from all NIH offices/persons responsible for recommendation implementation.

The Andersen, Inc. Management Tracking System, a relational database developed jointly by the DQM and the Office of Technology Transfer, NIH was the quality assurance tool NIH used to quantify all data related to the implementation of the Andersen, Inc. recommendations. An annual report from the Andersen Inc. Management Tracking System was issued to Congress via the DDM, and the Director, NIH, for inclusion in the Congressional Record.

Goal b) Improve the efficiency of the small acquisition process by continuing to expand the Purchase Card Program.

The Federal Supply Service of the General Services Administration (GSA) instituted the Purchase Card Program to help reduce the administrative burdens associated with making small purchases. The Purchase Card Program has been in effect at NIH since June, 1995. At NIH, this simplified acquisition method is used for purchases up to $2,500 where authorized and feasible.

The program is operated through NIH's Automated Data Base System (ADB), a computerized database that integrates acquisition, financial, and inventory information. This system gives purchase card holders the ability to review their purchases and credits, including fiscal year-to-date summary data, and provides approving officials with the ability to review the purchases and credits made by card holders and to perform transaction adjustments.

Expanded use of purchase cards by both scientific and administrative staff will reduce costs associated with procurement activities, expedite the acquisition of needed goods and services, and facilitate timely payment of bills. NIH's strategies for expanding the program include: 1) increasing the dollar volume of purchase card orders made by NIH staff, 2) increasing the number of NIH scientific and administrative staff trained to use purchase cards, 3) increasing the total number of NIH purchase card holders, and 4) increasing the number of annual purchase card orders/transactions.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Increase the dollar volume of purchase card orders made by NIH staff:					
$110 million in orders.	◆				
$160 million in orders.		◆			
$200 million in orders.			✖		
$210 million in orders.				◇	
$230 million in orders.					◇
Increase the number of NIH scientific and administrative staff trained to use purchase cards*:					
3,000 people trained to use cards.	◇→	◆			
3,600 people trained to use cards.		◇→	◆		
Increase the total number of NIH purchase card holders*:					
1,600 card holders.	◇→	◆			
2,000 card holders.		◇→	✖		
Increase the number of annual purchase card orders/transactions:					
365,000 orders/transactions.				◇	
395,000 orders/transactions.					◇

*Note: In FY 2001, NIH shifted its focus from training staff and increasing the number of card holders to the most important measures of performance for this program, dollar volume of purchase card orders and number of annual purchase card orders/transactions.

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **The Purchase Card Program expanded in terms of dollar volume.** The dollar volume of purchase card orders achieved in FY 1999 and FY 2000 exceeded targeted amounts by $20 million and $13 million, respectively. In FY 2001, the dollar volume increased to $196 million, but fell $4 million short of the target.

- **The number of staff trained to use purchase cards continued to increase.** Although the FY 1999 and FY 2000 targets to increase the number of staff trained to use purchase cards were not met, 2,860 staff members were trained by the end of FY 1999 and a total of 3,391 staff had been trained by the end of FY 2000. The number of staff trained to use the purchase card as of the end of FY 2001 was 3,922.

- **The number of purchase card holders has increased.** The FY 1999 through FY 2001 targets to increase the total number of NIH purchase card holders were not met, however the

numbers did increase each year. There were 1,485 card holders at the end of FY 1999, 1,729 card holders at the end of FY 2000 and 1,866 cardholders at the end of FY2001. This measure is not being used past FY 2001, however, as it is not considered a valid measure of the true staff involvement with the Program.

- **NIH seeks to increase the number of annual purchase card orders/transactions.** No performance has been reported to date. Reporting will begin in February 2003.

Verification/Validation of Performance Measures and Data Issues

When this goal was initiated, NIH decided to measure performance by the annual dollar volume of orders, the total number of staff trained to use the purchase cards, and the total number of purchase card holders. NIH used several means to verify the performance data, including Automated Data Base reports on purchase card transactions and records maintained by the NIH Office of Administration on the number of individuals trained and issued purchase cards.

Because the number of purchase cardholders has increased dramatically since the inception of this goal, future increases in the number of card holders may not be as significant in the future as it was in the past five years. Furthermore, it is difficult to estimate future requests for purchase cards. A request for a purchase card is at the discretion of each IC. Some IC's have internal directives on the usage of the purchase card.

At this point in the Purchase Card Program, the most meaningful measures of success focus on the annual dollar amount of orders and the annual number of orders/transactions generated. Performance data for these measures could be verified through Automated Data Base reports on purchase card transactions and dollar volume.

Goal c) Expand the use of Performance Based Contracting (PBC).

One of the major challenges for government management and administration is improving the efficiency and effectiveness of contracting and procurement activities. Historically, government policies, regulations, and attention have been directed at contracting for acquisitions of supplies rather than services. A 1997 OMB memorandum requires that all federal agencies use Performance Based Contracting (PBC) methods, where practicable, and match acquisition and contract administration strategies to specific requirements. In this way, PBC complements the government's overall emphasis on managing for results by linking payments to results rather than to effort or process.

PBC involves using performance requirements that define the work in measurable, mission-related terms, with performance standards of quality, quantity, and timeliness tied to those requirements. PBC also requires a quality assurance plan describing how the contractor's performance will be measured against the performance standards. In cases where a contract is either mission-critical or requires a large dollar amount, incentives are tied to the quality assurance plan measurements.

PBC provides NIH with useful indicators of contactor performance and allows vendors to be innovative in responding to requirements for specific products and services. NIH is therefore strongly committed to increasing the amount of NIH contracting dollars allocated to performance-based contracts. As new contract requirements and contract renewals arise, NIH will review each situation to determine if using PBC is appropriate.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Increase the amount of NIH contracting dollars allocated to performance-based contracts:					
Allocate $19.8 million of the available NIH contracting dollars to PBC-eligible contracts.		◆			
Allocate $21.2 million of the available NIH contracting dollars to PBC-eligible contracts.			◆		
Allocate $207.0 million of the available NIH contracting dollars to PBC-eligible contracts.[1]				◇	
Allocate $226.0 million of the available NIH contracting dollars to PBC-eligible contracts.					◇

[1] The nearly ten-fold increase in the dollar volume of the performance target in FY 2002 is primarily due to a single large performance-based contract awarded in FY 2000

◆ Target Met	◇ Target Active	◇⟶ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **The amount of contracting dollars allocated to PBC exceeded expectations.** NIH set $19.8 million as the initial performance target for allocating PBC-eligible contracts. In FY 2000, NIH significantly exceeded this target by allocating $198.5 million to PBC – more than 10 times higher than the targeted amount – due primarily to the award of a single, large, performance based contract. Using existing performance-based contracts and estimates of upcoming awards, the NIH set performance targets of $207 million in FY 2002 and $226 million in FY 2003 for PBC-eligible contracts.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the amount of contract dollars awarded. Performance data was verified through reports obtained from the Departmental Contracts Information System (DCIS).

Goal d) Identify and pilot new approaches to providing human resource services which increase manager satisfaction with personnel system flexibility and ease of use.

In 1997, NIH initiated a comprehensive evaluation, in conjunction with the National Academy of Public Administration (NAPA), to assess the utility and flexibility of NIH's personnel systems. This systematic assessment of the personnel system was warranted because NIH was faced with implementing many human resource services previously conducted by DHHS.

NAPA's 1997 baseline survey of NIH managers found that less than 20% viewed the personnel system as customer focused, less than 20% found the system flexible and easy to use, and only about 30% found the system contributed to organizational goals and objectives.

To improve the effectiveness of the personnel system, NIH has focused on 1) delegating human resource authorities to the ICs and 2) increasing managers' satisfaction with the systems' flexibility and ease of use. To that end, the NIH Director redelegated many of the personnel administration and management authorities to Institute Directors. In addition, managers and staff received training to ensure that they exercised the new authorities properly.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Delegate human resource authorities to the ICs:					
Complete the delegations of authority and related training.	◆				
Increase managers' satisfaction:					
A 10% increase in manager satisfaction with personnel system flexibility and ease of use as reflected in the 1999 survey outcome against the 1997 baseline.		◇→	→	◇	
Complete distribution of the final year management satisfaction survey, interviews, and collect and analyze data for the final report due in 2002.[1]			◇→	◇	

[1] This goal will be discontinued after FY 2002 to focus NIH's management/administration goals on the most significant issues.

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **Human resource authorities were delegated on schedule.** NIH met the FY 1999 target to complete the delegation of Title 5 authorities. In addition, the NIH Office of Human Resources Management (OHRM) conducted briefings for senior managers to inform them of the scope and content of the delegated authorities and of their responsibilities to

ensure that they are exercised in a proper manner. Managers and administrative staff who would be exercising the new authorities received more intensive briefings and training, including a series of training modules developed by OHRM. In addition, several ICs developed and implemented their own training procedures.

- **Determination of managers' satisfaction with the personnel system was delayed.** A final determination on manager satisfaction over the 5-year period of this pilot will be available in 2002. The initial results of the 1999 management survey showed a 6% increase in managers' satisfaction, compared to the baseline survey conducted in 1997. This increase fell short of the FY 2000 target to increase by 10% NIH managers' satisfaction with the personnel system's flexibility and ease of use.

Verification/Validation of Performance Measures and Data Issues

Performance will be measured by the completion of NAPA's 2001 survey of NIH managers, the analysis of the data gathered, and the issuance of the final report in 2002. Performance data will be verified through the survey and interview data maintained by NAPA and the final report.

The fifth and final year report is being completed and a report will be issued in 2002. Performance data will be verified through the survey and interview data collected by NAPA in the 2001 survey and contained in the final report.

Goal e) Recruit and retain highly qualified extramural investigators to biomedical/behavioral research through the use of student loan repayment programs.

To address the negative impact that staggering educational debt has on career choices for health professionals, NIH implemented several intramural Loan Repayment Programs (LRPs) to provide a financial incentive for highly qualified health professionals to join the NIH intramural research program. The LRPs are designed to attract highly qualified and diverse physician-scientists and bench researchers to the intramural research program by providing for the repayment of their educational loans, and to encourage these highly qualified health professionals to pursue a career in basic and/or clinical research at the NIH, other federal agencies, universities, teaching hospitals, or academic health centers. Through FY 2000, over 300 intramural researchers had benefited by having approximately $19 million of their educational debts repaid.

After the early and apparent success of NIH's intramural LRPs as recruitment and retention incentives, the extramural research community became interested in creating loan repayment programs to address other areas in need of biomedical/behavioral health professionals. In 1997, the Contraception and Infertility Research Loan Repayment Program became NIH's first LRP for extramural researchers. By 2001, Congress had authorized NIH to implement five extramural loan repayment programs (described below). These extramural LRPs are designed to encourage a diverse pool of highly qualified health professionals to engage in specific areas of inquiry, such as clinical research, pediatric research, contraceptive and infertility research, and minority health disparities research. Through its LRPs for extramural investigators, NIH hopes to enhance the recruitment of highly qualified health professionals, especially investigators who are early in their career, and also retain those health professionals as biomedical/behavioral researchers. Provided below are descriptions and activity codes for each of the LRP awards.

- **CIR – Contraception and Infertility Research Loan Repayment Program.** The CIR program provides an incentive for health professionals to conduct research related to contraceptive development and/or infertility diagnosis and treatment. The purpose of the program is to recruit highly qualified health professionals into these areas of reproductive research and to stimulate the commitment of those researchers to sustaining a career focus on contraception and/or infertility research.

  While participating in the CIR, individuals must be employed or training at an NICHD Intramural laboratory or eligible NICHD-supported extramural site. Eligible NICHD-supported extramural sites include: 1) Cooperative Specialized Contraception or Infertility Research Centers; 2) Cooperative Specialized Research Centers in Reproduction Research; 3) Women's Reproductive Health Research Career Development Centers; 4) reproductive medicine units identified as clinical or data-coordinating sites for the National Cooperative Reproductive Medicine Network, or 5) contraceptive clinical trial units identified as sites for

the Contraceptive Clinical Trials Network. These programs currently represent 56 awardee institutions and five consortium sites.

- **CR – Loan Repayment Program Regarding Clinical Researchers**. The CR program provides for the repayment of the educational loan debt of qualified health professionals who agree to conduct clinical research. The program provides for the repayment of up to $35,000 of the principal and interest of the educational loans of extramural grantees for each year of obligated service. The purpose of the CR is to recruit and retain highly qualified health professionals as clinical investigators.

- **ECR – Extramural Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds**. The ECR program provides an incentive for health professionals from disadvantaged backgrounds to conduct clinical research and an avenue for NIH to engage and promote the development of research programs that reflect the variety of issues and problems associated with disparities in health status. The program seeks to recruit and retain highly qualified health professionals from disadvantaged backgrounds into clinical research careers.

  An "individual from a disadvantaged background" is one who: (1) comes from an environment that [did little to encourage the individual in] obtaining the knowledge, skill and ability required to enroll in and graduate from a health professions school; or (2) comes from a family with an annual income below a level based on low-income thresholds according to family size published by the U.S. Bureau of the Census, adjusted annually for changes in the Consumer Price Index, and adjusted by the DHHS Secretary for use in all health professions programs. The Secretary periodically publishes these income levels in the Federal Register. Current financial need is not sufficient to classify an individual as being from a disadvantaged background.

- **HDR – Loan Repayment Program for Minority Health Disparities Research.** The HDR program provides an incentive for health professionals to engage in basic, clinical or behavioral research directly relevant to health disparities research. The program seeks to recruit and retain highly qualified health professionals in research careers that focus on minority health disparities research or research related to the medically underserved. In addition, pursuant to Public Law 106-525, 50 percent of the awards will be made to individuals from health disparities populations.

  This program emphasizes the recruitment of racial and ethnic minorities and other underrepresented individuals to conduct research because such emphasis "promotes a diverse and strong 21st century workforce" able to address society's diverse needs. The program enables NIH to support and facilitate the development of research programs that reflect an understanding of the variety of issues and problems associated with disparities in health status.

- **PR – Pediatric Research Loan Repayment Program.** The PR program provides for the repayment of the educational loan debt of qualified health professionals who agree to

conduct pediatric research. The program provides for the repayment of up to $35,000 of the principal and interest of the educational loans of extramural grantees for each year of obligated service. The purpose of the PR is to recruit and retain highly qualified health professionals as pediatric researchers.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Enhance recruitment of highly qualified health professionals, especially investigators who are early in their career:					
50% of eligible sites use the CIR for recruitment.				◇	
50% of applicants apply because of the opportunity to participate in the CIR.				◇	
15% of CR awardees are first time grant or other award recipients.				◇	
30% of ECR applicants are in training or have recently commenced their research careers.				◇	
30% of HDR applicants are in training or recently commenced their research careers.				◇	
15% of PR awardees are first time grant or other award recipients.				◇	
50% of HDR awardees are from health disparities populations.				◇	◇
75% of eligible sites use the CIR for recruitment.					◇
75% of applicants apply because of the opportunity to participate in the CIR.					◇
25% of CR awardees are first time grant or other award recipients.					◇
50% of ECR applicants are in training or have recently commenced their research careers.					◇
50% of HDR applicants are in training or recently commenced their research careers.					◇
25% of PR awardees are first time grant or other award recipients.					◇
Retain health professionals as biomedical/behavioral researchers:					
50% of past participants conduct contraception and/or infertility research two years after completing the CIR.				◇	
75% of past participants conduct contraception and/or infertility research two years after completing the CIR.					◇
50% of ECR awardees attend educational and/or technical assistance workshops, seminars and other educational mechanisms and are encouraged to apply for small grant support in their 2nd or 3rd year of the program.					◇
50% of HDR awardees attend educational and/or technical assistance workshops, seminars and other educational mechanisms and are encouraged to apply for small grant support in their 2nd or 3rd year of the program.					◇

◆ **Target Met** | ◇ **Target Active** | ◇⟶ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

NIH established this goal for FY 2002. Therefore, no performance has been reported to date. Initial reporting will begin in February 2003.

Verification/Validation of Performance Measures and Data Issues

Performance with respect to recruitment of researchers will be measured by the percent of applicants who are early in their research careers, the percent of awardees that are also first time recipients of an NIH grant or other award, the percent of eligible sites using the programs for recruitment, the percent of applicants seeking the programs, and the percent of awardees from specific populations. Performance with respect to retention of researchers will be measured by the percent of awardees that receive additional training and are encouraged to apply for small grant support, and the percent of participants retained in specific fields of study. The data will be drawn from the application and review processes. Performance data will be verified through reports from the Information for Management, Planning, Analysis, and Coordination (IMPAC) system and through reconciliation records maintained by the loan repayment program area.

Goal f) Implement government-wide initiative on delayering management levels and streamlining organization.

The goal of NIH research is to acquire new knowledge to help prevent, detect, diagnose, and treat disease and disability. At the same time, NIH is responsible for improving its management to further the success of its mission and research goals. To that end, NIH is working to implement five government-wide Presidential Management Initiatives aimed at:

- Strategic Management of Human Capital
- Expanding Electronic Government
- Competitive Sourcing
- Improve Financial Performance
- Budget and Performance Integration

To determine the best course of action for implementing these initiatives, an NIH Restructuring Committee was formed to make recommendations to the NIH Director. The committee's deliberations focused on the DHHS Secretary's vision of "One Department," views of DHHS senior staff, guidance from the Office of Management and Budget (OMB), and the recommendations of the Arthur Andersen, Inc. 1997 study of NIH administrative activities. The committee's recommendations, outlined in the NIH Restructuring Report, include centralizing the NIH Servicing Personnel Office, using the new NIH Business System as the model for implementing the Uniform Financial Management System, and supporting the development of Departmental Information Technology and Enterprise Human Resource Project systems.

In addition, NIH developed this performance goal focused on "delayering" or reducing the number of layers in management in an effort to streamline its organization. Reducing management layers will lessen the distance between citizens and decision-makers, thereby allowing NIH to be more responsive to public health needs. Specifically, NIH has undertaken a proactive compliance effort that focuses on two major activities: 1) identifying NIH organizational units where delayering may be possible, and 2) delayering those organizational units.

A preliminary review revealed that although NIH ICs require different organizational designs to meet their individual scientific objectives, five management layers (the Director, NIH, plus four at the IC level) is likely to be sufficient in most cases. However, certain complex organizational issues may preclude some ICs from effective performance under this management model. These issues include the organization of some intramural research laboratories that provide services through widely disbursed and mobile staff, and the size and scope of organizations such as NCI.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Identify NIH organizational units for possible delayering:					
Complete assessment of NIH organizational level structure and rationale for current patterns.				◇	
Identify organizational units for delayering.				◇	
Delayer NIH organizational units:					
Develop implementation plans to accomplish delayering for each organizational unit.				◇	
Develop specific numeric targets for the implementation plans.				◇	
Complete delayering for each organizational unit identified.					◇

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

NIH established this goal for FY 2002. Therefore, we have not reported any performance yet. We will begin initial reporting in February 2003.

Verification/Validation of Performance Measures and Data Issues

Performance data will be verified through organizational charts showing management layers before implementation, compared with organizational charts showing management layers after streamlining.

2.2 Research Training and Career Development Program

2.2.1 Program Description, Context, and Summary of Performance

Program Description and Context. The Research Training and Career Development Program addresses NIH's long-term goal to "promote the development of a suitable talent base of well qualified, highly trained, and diverse investigators capable of yielding the scientific discoveries of the future." To achieve this outcome, NIH provides training support through the National Research Service Award (NRSA) and various other types of career development programs. These programs are designed to increase the nation's ability to attract and retain the best and brightest minds in biomedical research and to develop a group of well-trained, highly skilled scientists who are ready to meet society's needs for health-related researchers. In addition, NIH's training and career development programs are aimed at enhancing the quality and diversity of the biomedical research labor force.

Predoctoral training. NIH research training and career development support is tailored to the needs of individuals at different career levels. At the predoctoral level, students who are beginning graduate training need to learn the conceptual and theoretical aspects of the science they hope to practice. For individuals at this level, the NIH supports broad, multidisciplinary training grants. This kind of support allows universities to assemble a sufficient number of students to justify the development of an educational curriculum in biomedical, behavioral, or clinical research. Students learn the fundamentals in a structured but competitive atmosphere that accelerates knowledge acquisition. These didactic experiences are usually supplemented with laboratory rotations that help define the frontiers of modern science and the methods used to address current research problems. Laboratory rotations also teach students that there are often a number of experimental approaches to a specific problem. Once students select a dissertation project, the content of training needs to change. In this phase of their studies, students operate primarily as apprentices, working on some aspect of a funded research project. Most biomedical graduate students receive support during this phase of their training by working as a research assistant on their mentor's research grant.

This approach to graduate training has been widely praised. The widely cited report, *Reshaping Graduate Education*, published in 1995 by the National Academy of Sciences (NAS), recommended that all federal agencies emulate this approach. Also, a recent NIH evaluation study found that individuals who received at least nine months of NRSA support during their predoctoral research training in the biomedical sciences are more likely to be employed by top-ranked academic institutions and are more likely to have been awarded a research grant by NIH or the National Science Foundation (NSF) than their colleagues who did not receive NRSA training. These NIH programs encourage academic institutions to provide high quality research training, and recipients of this support to make substantial contributions to the biomedical sciences.

Postdoctoral training. At the postdoctoral level, NIH supports an extension and expansion of the apprenticeship approach. For individuals who continue their formal education in the biological or behavioral sciences, NIH offers training grants, fellowships, and research assistantships to fund

this period of intense research activity. The primary focus at this level is on the acquisition of knowledge and skills necessary to launch an independent research career. For physicians and other clinicians with specialized skills and little training in health-related research, NIH offers career development awards that offer higher salaries, which are necessary to attract individuals who have completed training in other areas. These awards often include an initial didactic phase to provide instruction in the concepts the candidate will need as an independent researcher. The individual then proceeds to work as an apprentice on a specific project. In most cases, the candidate is ready to apply for his/her own research support by the end of the three- to five-year grant period.

Initiatives to increase diversity. All of the NIH ICs provide research training support through NRSA and/or other institutional and individual training awards. The ICs also use various award mechanisms to recruit individuals from racial and ethnic groups that are underrepresented in science. Every NIH research training grant must have a minority recruitment plan in place prior to award. Examples of awards designed to increase the diversity of the pool of research scientists are the Minority Access to Research Careers (MARC) and the Career Opportunities in Research (COR) programs. By funding research training experiences for undergraduate honor students at universities having a substantial minority enrollment, they serve an important role in attracting underrepresented students into careers in health-related research. Research Supplements for Underrepresented Minority Individuals permit high school, college, and graduate students; postdoctorates; and faculty members to work on an existing NIH research grant. Increasing the diversity of the research community is seen as an important factor in reducing the disparity in health outcomes observed in the U.S. population.

NIH is also concerned about the participation rates of women in biomedical and behavioral research. The issues associated with the involvement of women in research, however, differ substantially from that of underrepresented racial and ethnic groups. Women are close to parity with men in biomedical sciences at the graduate and postdoctoral levels. In behavioral science fields, women represent a clear majority of the training pool. However, women are underrepresented at the faculty level, with relatively few serving in high-level academic and administrative positions. They are also underrepresented among NIH principal investigators. NIH has initiated a number of programs to address this problem, including career development awards and administrative supplements to research grants to encourage fully trained scientists to re-enter research careers after taking time off to attend to family responsibilities.

NIH's Research Training and Career Development Program has one functional area, Training Support and Outreach. The performance goals and targets for this area are presented on the following pages, along with an introduction to each goal, verification/validation of the performance measures, and a summary of the performance results.

GPRA Research Training and Career Development Program					
Budget (dollars in thousands)	**FY 1999 Actual**	**FY 2000 Actual**	**FY 2001 Actual**	**FY 2002 Estimate**	**FY 2003 Request**
	$811,120	**$912,241**	**$1,023,475**	**$1,151,485**	**$1,247,741**

Summary of Performance – Research Training and Career Development Program

Comprehensive summary tables covering all the goals and targets in NIH's Research Training and Career Development Program follow. These tables provide updated information on the status of all of the program's performance targets for Training Support and Outreach activities. More extensive information on each goal, including a chart summarizing the performance results for each target, can be found at the referenced page number.

■ **TRAINING SUPPORT AND OUTREACH**			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
a) Respond to the National Academy of Sciences (NAS) quadrennial report on the future needs for health-related researchers.	**FY 2003** 1. Increase NRSA stipends 10% above the FY 2002 level. 2. Issue regulations that permit identification and data collection on graduate students and postdoctorates supported by research grants. 3. Deploy electronic appointment forms for graduate students and postdoctorates supported by research grants. --- **FY 2002** 1. Issue a statement to encourage universities to limit graduate training to 6 years and postdoctoral training to 5 years. 2. Increase NRSA stipends 10% above the FY 2001 level. 3 Develop regulations that permit identification and data collection on graduate students and postdoctorates supported by research grants.		Page 226

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	4. Develop electronic appointment forms for graduate students and postdoctorates supported by research grants. --- **FY 2001** Prepare response and implementation plans for the recommendations in the NAS report, *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists*. --- **FY 2000** Respond to the quadrennial assessment of the nation's future need for biomedical and behavioral research scientists issued on August 29, 2000 by the NAS.	--- A response to the Biomedical segments of the NAS report was issued on March 26, 2001. --- A statement in response to the NAS report was published in FY 2001 and is available on the NIH website.	
b) Maintain adequate application and award rates in key training support areas.	**FY 2003** 1. An application flow of 40% for fellowships (F32s). 2. An application flow of 60% for research training grants (T32s). 3. An application flow of 40% for career awards for basic scientists (K01s). 4. An application flow of 50% for entry-level career awards (K08s). --- **FY 2002** 1. An application flow of 40% for fellowships (F32s). 2. An application flow of 60% for research training grants (T32s). 3. An application flow of 40% for career awards for basic scientists (K01s). 4. An application flow of 50% for entry-level career awards (K08s). --- **FY 2001** 1. An application flow of 40% for fellowships (F32s). 2. An application flow of 60% for research training grants (T32s).	--- 1. The application flow for F32s was 45%. 2. The application flow for K01s was 42%.	Page 229

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	3. An application flow of 40% for career awards for basic scientists (K01s). 4. An application flow of 50% for entry-level career awards (K08s). 5. Monitor the need for new announcements and other outreach activities based on application rates, the age and accuracy of existing announcements, and informal assessments of information needs within the target applicant pool. --- **FY 2000** 1. An application flow of 40% for fellowships (F32s). 2. An application flow of 60% for research training grants (T32s). 3. An application flow of 60% for career awards for basic scientists (K01s). 4. An application flow of 60% for entry-level career awards (K08s). 5. Evaluate the effectiveness of the revised announcements, informational materials, and the new training website. --- **FY 1999** 1. An application flow of 40% for fellowships (F32s). 2. An application flow of 60% for research training grants (T32s). 3. An application flow of 60% for career awards for basic scientists (K01s). 4. An application flow of 60% for entry-level career awards (K08s). 5. Revise and publish announcements related to NIH research training and career	3. The application flow for T32s was 62%. 4. The application flow for K08s was 50%. 5. NIH monitored the monthly use of program announcements and policy documents available on the NIH training website. --- 1. The application flow for F32s was 48%. 2. The application flow for K01s was 36%. 3. The application flow for T32s was 67%. 4. The application flow for K08s was 50%. 5. Updated announcements for research training and career development programs were incorporated into the NIH training website. --- 1. The application flow for F32s was 44%. 2. The application flow for K01s was 37%. 3. The application flow for T32s was 64%. 4. The application flow for K08s was 52%. 5. Announcements for the F32, K01, K02, K05, K07, K08, K23,	

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	development opportunities. 6. Reissue the announcement for Minority and Disability Research Supplements. 7. Republish the booklet, *Research Training and Career Development Programs Supported by the National Institutes of Health*. 8. Re-announce programs as necessary to stimulate the submission of applications.	K24, and K30 awards were republished. 6. The announcements for these awards were published. 7. The final document was made available in FY 2000 on the NIH website. 8. NIH concluded that no additional announcements were needed because the standing programs continue to receive a sufficient number of applications.	
c) Increase the pool of clinician researchers trained to conduct patient-oriented research.	**FY 2003** 1. Issue at least 120 awards in the K23 (Mentored Patient-Oriented Research Career Development) category. 2. Maintain a steady state level of awards in the K24 category. --- **FY 2002** 1. Issue at least 120 awards in the K23 category. 2. Maintain a steady state level of awards in the K24 category. --- **FY 2001** 1. Issue at least 80 awards in the K23 category. 2. Issue at least 80 awards in the K24 category. --- **FY 2000** 1. Issue at least 80 awards in the K23 category. 2. Issue at least 80 awards in the K24 category. **FY 1999** 1. Re-announce the career award	 --- --- 1. 184 K23 awards were issued. 2. 58 K24 awards were issued. --- 1. 189 K23 awards were issued. 2. 75 K24 awards were issued. 1. The K23, K24, and K30	Page 233

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	components of the Director's Initiative on Clinical Research. 2. Issue at least 80 awards in the K23 category. 3. Issue at least 80 awards in the K24 category. 4. Issue at least 20 awards in the K30 (Clinical Research Curriculum Development Award) category.	programs were re-announced. 2. 85 K23 awards were issued. 3. 81 K24 awards were issued. 4. 35 K30 awards were issued.	
d) Increase the participation of underrepresented racial and ethnic groups, women, and individuals with disabilities in NIH training and research programs.	**FY 2003** Increase the number of individuals from underrepresented minority groups appointed to research training grants in FY 2001 at the predoctoral and postdoctoral levels. --- **FY 2002** Increase the number of individuals from underrepresented minority groups appointed to research training grants in FY 2000 at the predoctoral and postdoctoral levels. --- **FY 2001** 1. Continue to identify areas within the population of NIH-supported trainees that are not responding to efforts to increase demographic diversity. Develop remedial plans to address these problems as needed. 2. Establish a new paradigm for measuring the race/ethnicity of NRSA recipients to bring NIH into compliance with OMB guidelines. 3. Implement OMB-required race/ethnic data collection and reporting strategy.	--- 1. To identify problems with minority recruitment and retention, discussions were held with the NIH Training Advisory Committee, and an evaluation of the demographic diversity of NIH's existing training programs was initiated. Plans to address the problems will be completed in FY 2002. 2. The grant application form (PHS 398) and the fellowship application form (PHS 416) were modified to accept data using the two question race/ethnicity data collection approach. 3. NIH reached full compliance with OMB guidelines by providing a means for applicants to designate more than one race.	Page 235

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	FY 2000 Plan action as appropriate to identify and address demographic groups for which interest in training is abnormally low or declining. --- **FY 1999** 1. Issue a Notice of Proposed Rulemaking (NPRM) to permit part-time NRSA support and part-time payback options for individuals with pressing family obligations or disabilities. 2. Prepare a report identifying the demographics of the individuals supported by the NRSA mechanisms and career award mechanisms.	NIH determined that active enforcement of minority recruitment requirements on training grants and monitoring of participation rates was appropriate and will continue to enforce requirements and monitor participation. --- 1. The NPRM was published in the *Federal Register*. 2. Data were presented in a FY 2000 report. The data indicated that the diversity of the workforce is improving, but only very slowly.	
e) Expand capabilities for electronic administration of research training and career development activities.	**FY 2003** Receive at least 90% of all training appointments and termination information electronically. --- **FY 2002** Receive at least 50% of all training appointments and termination information electronically. --- **FY 2001** 1. All electronically received appointment information is used to establish trainee appointment records and personal profiles within the IMPAC II system. 2. At least 50% of all training appointments received electronically. **FY 2000** 1. Increase by 40% over the 1999 number of trainees, fellows, and career award recipients who maintain electronic records	--- 1. Changing technology limited NIH's progress. By December 2001, X-Train was deployed to eleven institutions and approximately 40 electronic appointment forms were received. NIH expects this system to be fully operational by the end of FY 2002. 2. Less than 5% of all training appointments were received electronically in 2001. Changing technology limited NIH's progress. The delay in implementing X-Train, which will	Page 238

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	for career tracking purposes in the NIH Person database. 2. Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies. 3. Increase by 40% over the 1999 number of trainee appointment forms received electronically.	operate under the NIH Commons, impacted the ability to complete all three FY 2000 targets. These targets are expected to be met in FY 2002 and will be reported on in February 2003**.**	
f) Improve the capabilities for career outcome tracking for NIH training and career development programs.	**FY 2003** 1. Identify resources to conduct ongoing evaluations of NIH research training programs employing data in the professional profile. 2. Use information from X-Train to establish a professional profile on 90% of all trainees. --- **FY 2002** 1. Develop a plan for ongoing evaluations of NIH research training programs employing data in the professional profile. 2. Develop and deploy X-Train, version 2.0 as a means of collecting appointment and termination information on NRSA recipients. 3. Develop capacity to use X-Train information to establish a professional profile for trainees. The professional profile will serve as a source of long-term career tracking information. --- **FY 2001** 1. Complete a report on the career outcomes of recipients of NIH extramural postdoctoral research training support. 2. Conduct an early evaluation of the K23 program based on focus groups composed of recipients.	--- 1. A preliminary report was in progress. Data sets were collected in FY 1999 and analyzed in FY 2000. 2. A focus group analysis of the K23 program was completed.	Page 241

■ TRAINING SUPPORT AND OUTREACH			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	FY 2000 1. Complete a report on the career outcomes of recipients of NIH extramural predoctoral research training support. 2. Initiate preliminary work on the long-term tracking database. --- **FY 1999** 1. Complete an evaluation study of NIH pre- and postdoctoral training programs based on existing data. 2. Add training activities functions to the NIH Commons.	1. NIH completed the report. 2. NIH could not establish the Professional Profile database because of delays in implementing the X-Train system. NIH expects this system to be fully operational by the end of FY 2002. --- 1. A report on NIH predoctoral training programs was completed in FY 2000. A preliminary report on the postdoctoral programs was in progress during FY 2001 and is expected to be completed by the end of FY 2002. 2. NIH could not add training activities functions because of delays in implementing the X-Train system. NIH expects this system to be fully operational by the end of FY 2002.	

2.2.2 Goal-by-Goal Presentation of Performance Goals and Results

2.2.2.1 Training Support and Outreach

The broad purpose of the NIH Training and Career Development Program is to enhance the nation's training programs at the predoctoral, postdoctoral, and early career developmental levels to ensure a continuing supply of capable individuals in areas of national need; encourage participants to pursue research careers; and foster the recruitment and retention of underrepresented groups into careers as researchers. Maintaining a highly trained population of scientists who can address the nation's future health-related research needs is an important task. To achieve this end, NIH offers a flexible and varied series of high-quality training opportunities, tailored to the career needs of recipients who are at different stages of education and career development. Some of these training opportunities are described below by activity code and name of award.

- **T32 -Institutional National Research Service (NRSA) Research Training Grant.** Institutional NRSA training grants provide support to academic institutions that can demonstrate a capacity to assemble a team of high-quality faculty and attract a suitable number of high-quality students or postdoctorates interested in engaging in a period of intensive, supervised research training. Training grants are an ideal way to support graduate students prior to their selection of a dissertation subject, allowing the students to consider scientific issues broadly and rotate through different laboratories to gain exposure to a variety of approaches to addressing research problems. Training grants also help students and postdoctorates learn the theories and practical aspects of research related to a particular disease or organ system. Special NRSA training grants support students in programs leading to a dual research degree, such as the M.D./Ph.D. degree.

- **T34 – Minority Access to Research Careers (MARC) and Career Opportunities in Research (COR).** MARC and COR training grants support undergraduate honor students at academic institutions having a substantial minority enrollment.

- **F31 - Individual NRSA Predoctoral Fellowship.** Predoctoral fellowships support supervised training at the graduate level. Special predoctoral fellowships provide support for disabled and minority graduate students.

- **F32 - Individual NRSA Postdoctoral Fellowship.** Postdoctoral fellowships support doctoral level scientists who need additional research experience to successfully compete for independent research funding. Fellows work as apprentices on a defined research project under the supervision of a sponsor or mentor.

- **K01 - Mentored Research Scientist Development Award.** The K01 award supports mentored career development experiences for fully-trained researchers who may have dropped out of research to attend to family responsibilities or who are switching to a new field of research.

- **K08 - Mentored Clinical Scientist Development Award.** The K08 award provides full-time salary support for individuals who have finished or nearly finished their clinical training and wish to pursue a career in research. Many K08 awardees are physicians who may have had very little prior research experience. The first phase of this award usually consists of a period of largely didactic experience, which is followed by closely supervised and project-focused learning experience. It is expected that most recipients of K08 awards will be ready to apply for independent research support by the end of the five-year award period.

- **K22 - Career Transition Award.** The K22 award is used to support the transition of postdoctoral researchers to an independent research position. Usually, the postdoctoral researcher applies without institutional affiliation. This award offers candidates provisional funding that is activated when a suitable independent research position is negotiated. Some of the K22 awards support a continuing period of postdoctoral experience that is followed by a period of independent research support. Career transition awards operate as a pilot program and NIH ICs use this award mechanism in different ways.

- **K23 - Mentored Patient-Oriented Research Career Development Award.** The K23 award is similar to the K08 award but focuses on research that involves human patients. This award is an important part of the Director's Initiative on Clinical Research that is described later in this section.

- **K24 - Midcareer Investigator Award in Patient-Oriented Research Award.** The K24 award provides up to half-time support for established investigators who want to serve as mentors for developing scientists to increase their capacity to conduct high quality patient-oriented research.

- **K30 - Clinical Research Curriculum Development Award.** The K30 award stimulates training in patient-oriented research by offering support to institutions for the development of curricula designed to provide the theoretical and conceptual understanding necessary for high-quality clinical research.

NIH uses these awards and several others (which are not shown) to help achieve its long-term goal of promoting the development of a suitable talent base of well qualified, highly trained, and diverse investigators capable of producing the scientific discoveries of the future. Planning is required, however, to ensure the continued success of the Research Training and Career Development Program. NIH's strategic planning focuses on the following four areas of responsibility:

- ***Estimating future needs for researchers.*** Estimating the nation's future workforce needs in the area of biomedical and behavioral research is difficult because it is almost impossible to accurately predict emerging public health needs and scientific opportunities. Executing a rapid response to changes in these areas is also difficult because of the long time period required for research training. To help address this challenge, NIH asks the National Academy of Science (NAS) to conduct a congressionally mandated study of the national

needs for health-related research personnel every four years, as required in Section 489 of the Public Health Act (P.L. 93-348). NAS released the eleventh edition of this series of reports, *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists*, on August 29, 2000. NIH uses the quadrennial NAS studies, expert panels, program evaluations, and other means to identify areas that should be addressed to improve its Research Training and Career Development Program.

After each NAS report is released, NIH thoroughly reviews the study and accompanying recommendations to plan the scope and focus of its various training and career development programs. Expert panels are also convened, as needed, to advise on specific issues. For example, in 1998, the NIH Director's Panel on Clinical Research identified a specific need to address current shortages of patient-oriented researchers. Targeted program evaluations, such as the recent NIH evaluation of the NRSA predoctoral fellowship program, provide additional information.

- ***Addressing future needs for researchers***. Given the inherent difficulties in estimating the future needs for researchers, the process for deciding the approximate number of NIH training and career development awards of each type to be given each year is challenging. Maintaining program continuity is an important consideration because research training often takes more than 10 years from the beginning of graduate school until the end of postdoctoral training. To retain the best students and to ensure that their training is of the highest quality, NIH tries to maintain a consistent level of support from year to year.

  Because students and postdoctoral researchers frequently select a number of different support options over the course of their training, it is important to make these options as attractive, predictable, and stable as possible. NIH monitors trends in application rates for specific awards to ensure that they remain attractive options and serve to recruit individuals into biomedical research careers. Improving outreach to increase awareness of the training opportunity, increasing the benefits for awardees, and/or increasing the probability of applicants being selected can enhance the attractiveness of an award. For mature programs that appear to be meeting the needs of NIH and the applicant pool, it is especially important to maintain fairly consistent award rates.

  In addition to offering a variety of awards and monitoring their attractiveness to individuals and academic institutions, NIH uses the quadrennial NAS studies, expert panels, and other means to identify areas that are not being adequately addressed by current training programs. For example, in response to the NIH Director's Panel on Clinical Research, NIH initiated the K23, K24, and K30 awards to address the identified shortages of patient-oriented researchers. Similarly, NIGMS recently launched a training program in bioinformatics and computational biology in response to emerging needs.

- ***Addressing issues associated with diversity and health disparities.*** NIH is strongly committed to training and supporting a research community that reflects the nation's racial and ethnic diversity. Accordingly, NIH offers a number of specific training awards (such as the previously mentioned MARC and COR research training grants and minority

supplements) that are designed to increase the diversity of the pool of research scientists. Different types of training programs are available at the graduate and postdoctoral levels to help ensure that individuals from underrepresented groups are retained throughout the period leading to their independence as research scientists. These programs are especially important as NIH attempts to reduce the disproportionately high incidence and prevalence of disease, burden of illness, and mortality experienced by certain groups, particularly racial and ethnic minorities. The involvement of representatives of all segments of the population within the research labor force should increase the likelihood that relevant health and research issues are addressed.

In addition to underrepresented racial and ethnic groups, NIH is interested in encouraging more women and individuals with disabilities to become successful research scientists. To achieve that end, NIH designed specific programs to address the retention of these groups in biomedical research careers. An important aspect of these efforts is monitoring of the demographics of the current workforce and the individuals participating in NIH training programs to assess needs and identify emerging problem areas.

- ***Maintaining high quality research training programs.*** A continuing effort is required to recruit bright, young scientists into biomedical research and maintain the effectiveness of NIH's training and career development programs. The key to maintaining high quality programs is peer review. NIH adjusts review criteria, as needed, and instructs peer reviewers to help identify the applications of institutions that are most likely to provide the best training and attract the best trainees.

  To assess the overall impact of the programs, NIH conducts periodic career outcome studies. These evaluations are coupled with external reviews, such as the quadrennial NAS studies. Together, such evaluations help ensure that NIH's Research Training and Career Development Program continues to be of high quality and sufficient magnitude to meet the nation's needs for biomedical and behavioral research. One of the needs identified in the 1993 NAS report, *Meeting the Nation's Needs for Biomedical and Behavioral Scientists*, concerned tracking and assessing the careers of training award recipients. In response to this recommendation, NIH launched a comprehensive evaluation of the predoctoral and postdoctoral NRSA training programs and is developing a web-based trainee appointment and tracking system, called X-Train, to facilitate future career outcome studies.

To address these challenges and enhance its training support and outreach efforts, NIH established six performance goals:

a) Respond to the National Academy of Sciences quadrennial report on future needs for health-related researchers.

b) Maintain adequate application and award rates in key training support areas.

c) Increase the pool of clinician researchers trained to conduct patient-oriented research.

d) Increase the participation of underrepresented racial and ethnic groups, women, and individuals with disabilities in NIH training and research programs.

e) Expand capabilities for electronic administration of research training and career development activities.

f) Improve the capabilities for career outcome tracking for NIH training and career development programs.

NIH's efforts to achieve the performance goals include designing and implementing a web-based trainee appointment and tracking system, maintaining adequately consistent application and success rates for NIH training programs, issuing an adequate number of awards to encourage patient-oriented research, monitoring and increasing the diversity of NIH-supported trainees, and evaluating the career outcomes of recipients of NIH fellowships and career development awards.

Performance Goal Details - Training Support and Outreach

Goal a) Respond to the National Academy of Sciences quadrennial report on the future needs for health-related researchers.

To achieve its goal of maintaining a highly trained population of scientists that can address the nation's health-related research needs, NIH must complete the difficult task of estimating the nation's future needs for researchers. To address this challenge, NIH asks the National Academy of Sciences (NAS) to conduct a congressionally mandated study of the national needs for health-related research personnel every four years. NAS released the eleventh edition of this series of reports, *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists,* on August 29, 2000. It is available on the NIH website at http://grants.nih.gov/training/nas_report/index.htm.

As part of this quadrennial study, NAS analyzes trends in the current labor force to anticipate future research needs, making specific recommendations about the size, quality, and the nature of NIH's training programs. The NAS studies have proven to be very useful in identifying special and continuing needs for biomedical, behavioral, and clinical scientists. NIH uses the NAS recommendations to make key decisions regarding the scope and focus of its training programs.

In addition to preparing a formal response to the most recent NAS report, NIH intends to improve its research training programs by focusing special attention on four of the NAS recommendations: 1) encouraging universities to expedite graduate and postdoctoral training, 2) increasing stipends paid to NRSA recipients, 3) issuing regulations for tracking the future careers of NIH trainees, and 4) designing and implementing a web-based trainee appointment system.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Formally respond to NAS recommendations for improving NIH research training programs:					
Respond to the quadrennial assessment of the nation's future need for biomedical and behavioral research scientists issued on August 29, 2000 by the NAS.		◇→	◆		
Prepare response and implementation plans for the recommendations in the NAS report, *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists*.			◆		
Encourage universities to expedite graduate and postdoctoral training:					
Issue a statement to encourage universities to limit graduate training to 6 years and postdoctoral training to 5 years.				◇	
Increase stipends paid to National Research Service Award (NRSA) recipients:					
Increase NRSA stipends 10% above the FY 2001 level.				◇	
Increase NRSA stipends 10% above the FY 2002 level.					◇
Issue regulations for tracking the future careers of NIH trainees:					
Develop regulations that permit identification and data collection on graduate students and postdoctorates supported by research grants.				◇	
Issue regulations that permit identification and data collection on graduate students and postdoctorates supported by research grants.					◇
Design and implement a web-based trainee appointment system:					
Develop electronic appointment forms for graduate students and postdoctorates supported by research grants.				◇	
Deploy electronic appointment forms for graduate students and postdoctorates supported by research grants.					◇

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **NIH formally responded to the NAS quadrennial report.** NIH officials reviewed the report, developed an initial implementation plan, and published a formal response to the biomedical segments of the report on March 26, 2001. The response stated NIH's intention to implement selected recommendations from the NAS report and will be updated after NIH has engaged the scientific community in a discussion on how to best implement these recommendations. To track the implementation of four of the most challenging NAS recommendations, NIH developed specific performance targets for FY 2002 and FY 2003, as shown in the above table.

- **NIH will encourage universities to expedite graduate and postdoctoral training**. Results of this effort will be reported in February 2003.

- **NIH plans to increase stipends paid to National Research Service Award (NRSA) recipients.** Results of this effort will be reported in February 2003 and 2004.

- **NIH is preparing to issue regulations for tracking the future careers of NIH trainees.** Results of this effort will be reported in February 2003 and 2004.

- **NIH is designing and implementing a web-based trainee appointment system.** Results of this effort will be reported in February 2003 and 2004.

Verification/Validation of Performance Measures and Data Issues

Performance was demonstrated by NIH's submission to Congress of its formal response to the NAS quadrennial report and the development of GPRA performance targets for four of the most challenging NAS recommendations. Verification of performance is available through public documents, including the online posting of NIH's formal response to the NAS quadrennial report (http://grants.nih.gov/training/nas_report/NIHResponse.htm).

Goal b) Maintain adequate application and award rates in key training support areas.

As the preeminent biomedical research program in the world, NIH attracts a high number of applications each year to its prestigious Research Training and Career Development Program. The overall goal of this program is to maintain a population of scientists who are well educated, highly trained, and dedicated to meeting the nation's future health-related research needs. At the same time, NIH must monitor application and award rates constantly to improve the Research Training and Career Development Program and make certain it is addressing the nation's needs.

NIH's efforts to maintain adequate application and award rates (also called success rates) are focused on 1) comparing application and success rates for the most popular awards to historical rates, and 2) conducting needed training and career development outreach activities.

Application rates for NIH training and career development programs are rough but important indicators of the continuing attractiveness of these programs to the research community. If an application rate falls below historical rates, NIH determines the reason and responds accordingly. For example, NIH can enhance the attractiveness of a particular award by increasing applicants' probability of success (the award rate), increasing benefits for awardees, or improving outreach.

Award rates affect the attractiveness of an award since applicants who think they are unlikely to receive an award may opt for other sources of support. It is therefore important for NIH to maintain some stability in the overall success rate so that applicants know what to expect. Comparing current application and award rates with historical rates provides NIH staff with the critical information they need to determine whether the eligibility criteria or provisions of an award should be adjusted.

NIH uses a combination of outreach efforts to inform prospective applicants about careers in research and the availability of financial support, which help maintain adequate application rates. Outreach activities of the Research Training and Career Development Program include the following:

- NIH training staff attend national conferences on biomedical research and other scientific meetings to encourage students and postdoctorates to engage in training leading to a career in biomedical research.

- The NIH homepage (http://www.nih.gov/) averages more than 7 million hits per month and is one of the most frequently accessed websites in the federal government. The homepage for NIH Research Training Opportunities (http://grants.nih.gov/training/index.htm) is the sixth most frequently hit page and constitutes an important and growing part of NIH's outreach effort.

- The NIH Research Training Opportunities homepage has links to the extramural training website (http://grants.nih.gov/training/extramural.htm), which contains a link to a popular online booklet, *Research Training and Career Development Programs* (http://grants.nih.gov/training/careerdev/intro.html). The booklet is organized by academic and career levels and is designed to help all interested parties – from high school students through postdoctorates – locate information about NIH-funded programs.

- NIH announces all grant opportunities online in the *NIH Guide to Grants and Contracts* (http://grants.nih.gov/grants/guide/index.html), which provides information on research, research training, and career development opportunities in both the intramural and extramural programs. The website organizes the information in the *NIH Guide* into a logical format so potential applicants will have all the information needed to apply for NIH programs. Any interested researcher can receive this electronic document each week by signing up for the extensive listserve.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Compare application and success rates for the most popular awards to historical rates:					
An application flow of 40% for fellowships (F32s).	◆	◆	◆	◇	◇
An application flow of 60% for research training grants (T32s).	◆	◆	◆	◇	◇
An application flow of 60% for career awards for basic scientists (K01s).	✖	✖			
An application flow of 60% for entry-level career awards (K08s).	✖	✖			
An application flow of 40% for career awards for basic scientists (K01s).			◆	◇	◇
An application flow of 50% for entry-level career awards (K08s).			◆	◇	◇
Conduct needed training and career development outreach activities:					
Revise and publish announcements related to NIH research training and career development opportunities.	◆				
Reissue the announcement for Minority and Disability Research Supplements.	◆				
Republish the booklet, *Research Training and Career Development Programs Supported by the National Institutes of Health*.	◇→	◆			
Re-announce programs as necessary to stimulate the submission of applications.	◆				
Evaluate the effectiveness of the revised announcements, informational materials, and the new training website.		◆			
Monitor the need for new announcements and other outreach activities based on application rates, the age and accuracy of existing announcements, and informal assessments of information needs within the target applicant pool.[1]			◆		

[1] Monitoring the need for new announcements and other outreach activities has become a routine activity and was therefore discontinued as an explicit target after FY 2001.

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **NIH continues to maintain application and success rates for the most popular awards that are comparable to historical rates.** In both FY 1999 and FY 2000, NIH received sufficient numbers of applications to maintain a consistent contribution to the support of training in the health-related sciences. The continuously high application rates indicate that the programs have remained popular with the pool of potential applicants. The award rates for individual fellowships (F32s), institutional research training grants (T32s), and mentored research scientist and clinical scientist development awards (K01s and K08s) were also sufficiently close to their historical rates, indicating that the quality of applications has remained stable.

  In FY 2000, the F32 and T32 award rates (48% and 67%, respectively) exceeded the corresponding target rates of 40% and 60%. The K01 and K08 award rates (36% and 50%, respectively) both fell short of the 60% target rate, and a subsequent analysis indicated that the 60% rate was unrealistically high for these career development awards. Beginning in FY 2001, the K01 and K08 target award rates were revised downward to 40% for K01 awards and 50% for K08 awards. In FY 2001, the success rates for F32s (45%), K01s (43%), K08s (50%) and T32s (62%) were all very close to target rates. NIH will continue to monitor the application and award rates for all of these programs each year, taking steps to re-announce specific programs and/or change some of their features if NIH observes trends that would warrant such action.

- **NIH conducted needed training and career development outreach activities.** During FY 2001, the need for new announcements and other outreach activities was assessed informally at two regional seminars (one held in Portland, Oregon and one in Honolulu, Hawaii) and at a variety of scientific conferences and conventions. Although there was no demonstrated waning of interest in NIH training and career development programs, plans were implemented to update the T32 and career awards program announcements in FY 2002.

  During FY 1999, NIH met three of the four targets in this area. Specifically, NIH revised and reissued announcements for the F32, K01, K02, K05, K07, K08, K23, K24, and K30 awards; reissued announcements for the Minority and Disability Supplement awards in May 1999; and determined that the application rates for the most popular programs were close to historical levels and did not require re-announcements. NIH also completed a draft copy of the on-line booklet, *Research Training and Career Development Programs Supported by the National Institutes of Health*, in FY 1999 and posted the final document on NIH's new training website in FY 2000.

  NIH met the FY 2000 target to evaluate the effectiveness of the revised announcements, informational materials, and the new training website. NIH included updated announcements for research training and career development programs on the NIH training website. The program announcements and policy documents available through this venue continue to receive substantial monthly use.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the annual application and success rates for T32, F32, K01, and K08 awards and by assessments of the information needs of potential applicants. Performance data were verified through reports generated from the IMPAC database system and information obtained using WebTrends site analysis software.

Goal c) Increase the pool of clinician researchers trained to conduct patient-oriented research.

NIH is committed to increasing the number of physicians and other clinicians trained to conduct patient-oriented research, and it recently implemented three new career mechanisms to achieve this important goal. These three mechanisms are components of the Director's Initiative on Clinical Research.

Increasing clinicians' expertise in conducting patient-oriented research was strongly recommended by two prestigious groups – an NIH Director's Panel on Clinical Research, and an Institute of Medicine (IOM) Committee on Addressing Career Paths for Clinical Research. Both groups recommended that NIH expand and improve its training programs in patient-oriented research for both entry-level and mid-career clinical investigators so that these researchers could capitalize on recent discoveries based on molecular approaches and translate them to clinical settings.

Accordingly, NIH established three new career development mechanisms designed to issue an adequate number of awards to encourage patient-oriented research. The first mechanism is the *Mentored Patient-Oriented Research Career Development Awards* (K23) to support young investigators. The second mechanism is the *Midcareer Investigator Award in Patient-Oriented Research Awards* (K24) to support mid-career investigators in research and mentoring. The third is the *Clinical Research Curriculum Development Awards* (K30) to enhance curriculum development in clinical research. All three award mechanisms appear to be attractive to potential applicants, and NIH expects that they will eventually increase the number of productive scientists working in this important area.

To convey NIH's commitment to training in this area in future years, the Director's Initiative recommended that at least 80 K23 and 80 K24 awards be made each year from FY 1999 through FY 2003 to achieve a steady state of approximately 400 awards of each type. Annual performance targets were accordingly developed for K23 and K24 awards, along with a target to issue at least 20 curriculum development (K30) awards in FY 1999. The K30 target was discontinued in future years.

After the five-year initial period, NIH will examine the continuing need for this program and will set new targets if necessary. After five years' experience, it may be possible to develop routine procedures for managing the application rate through announcements and changes in award provisions, thereby achieving a stable success rate.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Issue an adequate number of awards to encourage patient-oriented research:					
Re-announce the career award components of the Director's Initiative on Clinical Research.[1]	◆				
Issue at least 20 awards in the K30 category.	◆				
Issue at least 80 awards in the K23 category.	◆	◆	◆		
Issue at least 80 awards in the K24 category.	◆	✖	✖		
Issue at least 120 awards in the K23 category.				◇	◇
Maintain a steady state level of awards in the K24 category.				◇	◇

[1] Reannouncing awards to encourage patient-oriented research has become a routine activity and was therefore discontinued as an explicit target after FY 1999.

◆ Target Met	◇ Target Active	◇⟶ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **NIH continues to issue awards to encourage patient-oriented research.** In FY 1999, NIH re-announced three components of the Director's Initiative on Clinical Research (the K23, K24, and K30 awards) and subsequently issued 85 K23 awards, 81 K24 awards, and 35 K30 awards during the fiscal year, meeting all of the targets. In FY 2000, NIH issued 189 K23 awards (more than twice the targeted level) and 75 K24 awards (slightly less than the targeted level).

  In FY 2001, NIH issued 184 new K23 awards (again, greatly exceeding the target of 80 awards) and 58 K24 awards (fewer than expected). The K24 results suggest that the pool of mid-career patient-oriented researchers has been saturated and the annual performance target for K24 awards should be revised downward in future years. The shortage of individuals available for mid-career awards was identified in the report on the Director's Initiative on Clinical Research. Considering the unexpectedly high number of K23 awards in FY 2000 and 2001, NIH has revised the annual performance target upward for this award targeting younger scientists.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the number of annual K23 and K24 applications and awards. Performance data were verified through reports generated from the IMPAC database system.

Goal d) Increase the participation of underrepresented racial and ethnic groups, women, and individuals with disabilities in NIH training and research programs.

NIH believes strongly that training and supporting a research community that reflects the nation's social diversity is a top priority, and it is developing programs to monitor and increase the diversity of NIH-supported trainees.

Accordingly, NIH is designing a number of training programs to provide support to minority graduate and postdoctoral students and to recruit them into research at all career levels. NIH also is developing programs designed to enhance the retention of women in biomedical research careers and provide support for individuals with disabilities. All of these efforts address, in part, the disparities in morbidity and mortality across racial/ethnic and other demographic groups. Continual monitoring of the demographics of the participants in NIH programs is an important aspect of these efforts. This ongoing vigilance permits NIH to assess the value of existing initiatives and identify emerging problem areas.

NIH is particularly interested in implementing OMB's revision of Directive 15 (for details see http://www.whitehouse.gov/OMB/inforeg/race.pdf) related to collecting data on race and ethnicity. Under these new guidelines, all Federal agencies must collect information on ethnicity separately from race, and all agencies must offer respondents the option of indicating more than a single race. OMB offered recommendations for reporting the new data. As NIH moves toward compliance with the new guidelines, it needs to modify data collection forms such as the Statement of Appointment Form (Form 2271), the Grant Application Form (Form 398), and the Individual Fellowship Application (Form 416-1). In addition, NIH has to modify the data entry screens for IMPAC II and the underlying data structures to accept the new data. Finally, NIH has to design and approve reporting conventions that adjust for discontinuities in the nature of race/ethnic data.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Develop programs to monitor and increase the diversity of NIH-supported trainees:					
Issue a Notice of Proposed Rulemaking (NPRM) to permit part-time NRSA support and part-time payback options for individuals with pressing family obligations or disabilities.	◆				
Prepare a report identifying the demographics of the individuals supported by the NRSA mechanisms and career award mechanisms.	◇→	◆			
Plan action as appropriate to identify and address demographic groups for which interest in training is abnormally low or declining.		◆			
Continue to identify areas within the population of NIH-supported trainees that are not responding to efforts to increase demographic diversity. Develop remedial plans to address these problems as needed.			◇→	◇	
Establish a new paradigm for measuring the race/ethnicity of NRSA recipients to bring NIH into compliance with OMB guidelines.			◆		
Implement OMB-required race/ethnic data collection and reporting strategy.			◆		
Increase the number of underrepresented minorities appointed to research training grants:					
Increase the number of individuals from underrepresented minority groups appointed to research training grants in FY 2000 at the predoctoral and postdoctoral levels.				◇	
Increase the number of individuals from underrepresented minority groups appointed to research training grants in FY 2001 at the predoctoral and postdoctoral levels.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH made progress in developing programs to monitor and increase the diversity of NIH-supported trainees.** NIH met the first FY 1999 target on schedule by issuing a Notice of Proposed Rulemaking (NPRM) for 42 Part 66, which NIH published in the *Federal Register* on June 30, 1999. The NPRM addressed the needs of young women especially, as well as others with pressing family obligations or disabilities, by permitting NIH to award part-time NRSA support and part-time payback options. The final rule was published on May 31, 2001 and is available at http://grants.nih.gov/training/nrsa.htm. For the second FY 1999 target, NIH developed programs to extract race/ethnicity data on individuals supported by NRSA and other career development programs, but the analysis was not completed until FY 2000. The data presented in the FY 2000 report indicated that the diversity of NIH trainees is slowly improving. In addition, NIH met the related FY 2000 target to plan action as appropriate to identify demographic groups for which interest in training is abnormally low or declining. NIH has continued to enforce minority recruitment requirements actively for T32 research training grants and monitor the participation of individuals from underrepresented groups.

In FY 2001, several steps were taken to identify and address problems involving minority recruitment and retention. In addition to in-depth discussions initiated by the NIH Training Advisory Committee, the NIH National Center on Minority Health and Health Disparities (NCMHD) engaged the National Research Council in a broad study to evaluate the demographic diversity of NIH's existing training programs. Both initiatives were designed to identify successful programs as well as those that may require remedial action. Plans to address these problems will be completed in FY 2002.

NIH met the other two FY 2001 targets that involved the development and implementation of an improved system for measuring the race/ethnicity of NRSA recipients, as required by OMB. Specifically, NIH successfully established a new paradigm for collecting race/ethnicity data using two questions rather than one, and modified the grant application form (PHS 398) and fellowship application form (PHS 416) to reflect the new approach. The modified forms also permitted applicants to designate more than one race, bringing NIH into full compliance with OMB guidelines. In addition, underlying data structures were modified to accept data using the new approach.

- **NIH will seek to increase the number of underrepresented minorities appointed to research training grants.** Results of this effort will be reported in February 2003.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by tracking the participation of individuals of different races and ethnicities in NIH research and training programs. However, because only 75-85 percent of applicants generally respond to questions about their race and ethnicity, accurate measures of participation are difficult to obtain. NIH is working to improve the response rates by redesigning grant and fellowship application forms and providing applicants with better explanations of why they should complete this voluntary portion of the application. NIH uses several means to verify performance data, including reports on the year-end status of new procedures for identifying race/ethnicity, records maintained by the Research Training and Career Development Program, and reports generated from the IMPAC database system.

Goal e) Expand capabilities for electronic administration of research training and career development activities.

NIH is developing new electronic capabilities to improve and streamline the reporting, processing and analyzing of training and career development data, and to greatly expand its career-tracking capabilities. This electronic administration system will be more effective and efficient than the current system; it will provide access to richer data on training experiences and career outcomes, and it will facilitate better evaluations of NIH training programs. To enhance the quality of these programs, electronic administration will also be used to match the performance of former trainees and fellows to specific characteristics of their training programs. As a result, NIH should be able to respond better to the constantly changing national needs and priorities for research training.

To expand its capabilities for electronic administration, NIH is focusing on two major activities: 1) furthering the development of NIH's web-based trainee appointment system, and 2) increasing electronic receipt of trainee appointment and termination information. Further development of a web-based interface for electronic submission of trainee appointment and termination information will facilitate reporting by recipient organizations that receive NRSA institutional training grants. This electronic system will be part of the NIH electronic Research Administration system (eRA) and will improve the ease of data entry and processing, in addition to improving the quality of data. The specific features of this system, referred to collectively as the Electronic Trainee Activities System (X-Train), are still in the development stage. A link to the future X-Train system is available on the NIH Commons website at https://www-commons.cit.nih.gov/.

During FY 2000, NIH made little progress in improving the capabilities of X-Train due to several problems, including integrating electronic appointment information with the Professional Profile database. When completed, the Professional Profile will serve as a repository of biographical information on all individuals affiliated with NIH either as principal investigators, key personnel, trainees, fellows, or career award recipients. By encouraging all affiliated scientists to continually update their web-based biographical information, NIH will be able to improve its analyses of the effect of training support on career outcomes. The database will have the capability to track scientists' academic positions, publications, appointments to advisory groups, and grant awards.

For more than four years, NIH has been working on mechanisms to increase electronic receipt of information about trainee appointments and terminations. In FY 1997, NIH established a precursor system to X-Train and demonstrated the value of electronic administration of research training and career development activities. Using that system, NIH received 614 trainee appointment forms electronically. In FY 1998, NIH received more than 1,029 forms electronically, a 68 percent increase over the previous year. In FY 2001, 15 Federal Demonstration Partnership institutions will test the new system, and NIH expects to have this interface fully operational by the end of FY 2002. Expanding the operation of this system during

FY 2003 to all institutions with NRSA training grants will increase the volume of electronic information dramatically.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Further develop NIH's web-based trainee appointment system (X-Train):					
Increase by 40% over the 1999 number of trainees, fellows, and career award recipients who maintain electronic records for career tracking purposes in the NIH Person database.		◇	→	◇	
Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies.		◇	→	◇	
All electronically received appointment information is used to establish trainee appointment records and professional profiles within the IMPAC II system.			◇ →	◇	
Increase electronic receipt of trainee appointment and termination information:					
Increase by 40% over the 1999 number of trainee appointment forms received electronically.		◇	→	◇	
At least 50% of all training appointments received electronically.			◇ →	◇	
Receive at least 50% of all training appointments and termination information electronically.				◇	
Receive at least 90% of all training appointments and termination information electronically.					◇

◆ Target Met | ◇ Target Active | ◇ → Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **Changing technology limited NIH progress in developing its web-based trainee appointment system.** In FY 2000, the need to adapt to changing technology, finalize the resource allocation processes, and address the need for compatibility with other federal systems delayed the implementation of the X-Train system. However, NIH succeeded in deploying an early version of X-Train to two institutions on October 1, 2001. A total of eleven institutions were using X-Train by December 1, 2001 and a total of 36 appointment forms had been obtained electronically by December 1. Plans are in place to solicit comments from external users and expand the system to the approximately 200 institutions with training grants by the end of FY 2002. The X-Train system will also be updated in FY 2002 as the NIH Commons architecture is revamped with J2EE technology. By the end of FY 2002, NIH expects X-Train and the related Professional Profile database to be fully operational and capable of handling nearly all appointment and reappointment information for NRSA recipients. This system will also receive nearly all termination information on NRSA recipients unless the trainee's signature is required to verify a service payback obligation.

Due to the delay in implementing X-Train, NIH did not meet the FY 2000 targets to increase the number of trainees, fellows, and career award recipients who maintain electronic records and to develop a long-term plan to evaluate NIH research training programs. NIH's overall approach to future evaluations of the research training programs will depend on the web-based appointment data collected via X-Train, which is not expected to be available until FY 2002. At that time, NIH will know more about the nature and reliability of the electronic information in X-Train and, as a result, will be better equipped to plan effective evaluations.

- **Unexpected delays were experienced in increasing the electronic receipt of trainee appointment and termination information.** Due to the unexpected delay in implementing the X-Train system, NIH made little progress in FY 2000 to increase the amount of trainee appointment and termination information received electronically. NIH does not expect to meet the FY 2000 and FY 2001 targets until FY 2002. By the end of FY 2002, nearly all NRSA trainee appointments should be received electronically.

Verification/Validation of Performance Measures and Data Issues

Performance will be measured by the number of appointment forms and termination notices received electronically and by the year-end status of evaluation plans for NIH research training programs. All electronic appointment forms received via X-Train will be used to establish a professional profile that NIH will use for tracking career outcomes. A temporary database will hold each electronic form received until the NIH official responsible for the training grant has reviewed and approved its contents, after which it will be added to the IMPAC database system. Performance data will be verified through records maintained by the Research Training and Career Development Program and through reports generated from the IMPAC system.

Goal f) Improve the capabilities for career outcome tracking for NIH training and career development programs.

NIH recognizes the importance of developing, managing, and improving its training and career development programs based on sound knowledge about their effectiveness. To improve its capabilities for gathering this knowledge, NIH has focused its effort on two major activities: 1) evaluating the career outcomes of recipients of NIH fellowships and career development awards, and 2) expanding the X-Train system to establish a professional profile on all NIH trainees.

NIH has undertaken several evaluations of career outcomes related to its research training and career development awards. For example, NIH recently initiated a comprehensive tracking effort to evaluate career outcomes of the National Research Service Award (NRSA) programs for both predoctoral and postdoctoral research training. The evaluations were designed to examine how many NRSA recipients apply for and receive subsequent NIH fellowship support, apply for and receive subsequent NIH research grant support, publish in peer-reviewed journals, and remain in scientific careers.

During FY 2001, NIH conducted an early assessment of the effectiveness of the Mentored Patient-Oriented Research Career Development Award (K23) program. The purpose of this assessment was to identify through focus groups which career development experiences are related to successful career outcomes. The findings should be useful in improving review criteria and monitoring awards.

To establish a professional profile on all NIH trainees, NIH plans to enhance the Electronic Trainee Activities System (X-Train). In FY 2001, NIH will begin expanding X-Train to include a long-term career tracking mechanism for NRSA-supported individuals, using data from the related Professional Profile database. By 2002, NIH hopes to extend tracking to predoctoral and postdoctoral research assistants, providing valuable information about the post-award careers of NIH recipients of training support.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Evaluate the career outcomes of recipients of NIH fellowships and career development awards:					
Complete an evaluation study of NIH pre- and postdoctoral training programs based on existing data.	◇→	→	→	→◇	
Complete a report on career outcomes of recipients of NIH extramural predoctoral research training support.		◆			
Complete a report on career outcomes of recipients of NIH extramural postdoctoral research training support.			◇→	→◇	
Conduct an early evaluation of the K23 program based on focus groups composed of recipients.			◆		
Develop a plan for ongoing evaluations of NIH research training programs employing data in the professional profile.				◇	
Identify resources to conduct ongoing evaluations of NIH research training programs employing data in the professional profile.					◇
Expand the X-Train system to establish a professional profile on all NIH trainees:					
Add training activities functions to the NIH Commons.	◇→	→	→	→◇	
Initiate preliminary work on the long-term tracking database.		◇→	→	→◇	
Develop and deploy X-Train, version 2.0 as a means of collecting appointment and termination information on NRSA recipients.				◇	
Develop capacity to use X-Train information to establish a professional profile for trainees. The professional profile will serve as a source of long-term career tracking information.				◇	
Use information from X-Train to establish a professional profile on 90% of all trainees.					◇

◆ **Target Met** | ◇ **Target Active** | ◇→ **Target Not Met and Extended** | ✖ **Target Not Met**

Summary of Performance Results

- **NIH made progress in evaluating the career outcomes of recipients of NIH fellowships and career development awards.** For efficiency purposes, NIH divided the FY 1999 target to complete a comprehensive evaluation of pre- and postdoctoral training programs into two studies. One study focused on the career outcomes of predoctoral NRSA recipients and the other study focused on the career outcomes of postdoctoral NRSA recipients. NIH made progress on both evaluations but neither study was completed in FY 1999, as originally planned. However, NIH produced a draft report in FY 1999 of the first study, *The Early Career Outcomes of NRSA Predoctoral Trainees and Fellows.* The FY 2000 target was completed on schedule with the issuance of the final report for the study. The predoctoral evaluation found that individuals who receive at least nine months of NRSA support for predoctoral research training in the biomedical sciences are more likely to be employed by top-ranked academic institutions and are more likely to have received an NIH or NSF

research grant than their colleagues without NRSA training. For the postdoctoral study, NIH compiled data sets in FY 1999 and analyzed them in FY 2000. NIH expects the preliminary report of the postdoctoral study to be completed in December 2001 and the final report to be completed by the end of FY 2002.

With respect to the K23 program evaluation, focus group analyses were completed on schedule in FY 2001 and the results are posted on the Research Training and Career Development Program website.

- **NIH experienced delays in expanding the X-Train system to establish a professional profile on all NIH trainees.** The X-train software was available for internal testing for several months in FY 1999, but NIH could not establish the Professional Profile database in FY 2000 as a source of long-term tracking information because of delays in implementing the X-Train system. By the end of FY 2001, X-Train version 1.5 had been deployed in a limited fashion, and information from the limited pool of users should be useful in enhancing the system. By the end of FY 2002, NIH expects that a mature version of X-Train system and the related Professional Profile database will be operational, permitting the establishment of a professional profile on all NIH trainees.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the year-end status of current and planned evaluations and reports of NIH research training programs and by the year-end status of the X-Train system. Verification of performance is available through records maintained by the Research Training and Career Development Program and through reports generated from the IMPAC database system.

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2.3 Research Facilities Program

2.3.1 Program Description, Context, and Summary of Performance

Program Description and Context. NIH's Research Facilities Program addresses its long-term goal to "secure facilities for research that are modern, efficient and safe." This core program has two functional areas: (1) Intramural Modernization and Improvements, and (2) Extramural Assistance.

Intramural Modernization and Improvements. NIH has over 11 million gross square feet of federally owned facilities, which must keep pace with the demands of rapidly changing technologies and priorities in biomedical and behavioral research. It maintains over 70 buildings located on the main NIH campus in Bethesda, Maryland and additional facilities on the National Institute of Environmental Health Science (NIEHS) campus in Research Triangle Park, North Carolina. NIH also maintains several off-campus field stations, including the NIH Animal Center in Poolesville, Maryland; the Frederick Cancer Research and Development Center at Fort Detrick in Frederick, Maryland; the Gerontology Research Center in Baltimore, Maryland; and the Rocky Mountain Laboratory in Hamilton, Montana and New Iberia, Louisiana.

Construction of NIH buildings and facilities began more than 60 years ago, dating back to the June 1936 legislation that authorized Building 1 on the Bethesda campus. In fact, most of NIH's intramural facilities were constructed decades ago. As a result, NIH is contending with an aging physical plant. Many buildings, facilities, and utility systems have reached or are nearing the end of their useful life. In addition, the emergence of new technologies, the evolving scope of medical research, and a variety of other factors lead to facility obsolescence and the need for modernization and replacement of facilities. Managing these capital assets is integral to the success of the NIH intramural research program in achieving its research goals and the national health goals established by DHHS.

NIH's Intramural Modernization and Improvements Program (IMIP) facilitates the development of annual facility planning, programming, budgeting and construction execution strategies, which include the energy reduction objectives of the National Energy Conservation Policy Act and Executive Order 13123, compliance with Executive Order 13148, Greening the Government Through Leadership in Environmental Management, as well as other facility management initiatives. The IMIP is the product of a systematic process of interaction between the facility planning, programming, design and construction components of NIH and the various ICs. Other program inputs include technologically-driven protocols and advancements; facility assessments and surveys; engineering studies; compliance with building, environmental, and other regulatory requirements; accreditation guidelines of the Association of Assessment and Accreditation of Laboratory Animal Care International (AAALAC) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) that identify the programmatic and operating requirements for the patient care and research environment; politically-driven research initiatives; and recommendations of the approved NIH Facilities Master Plan.

Requirements of the Buildings and Facilities (B&F) program are reviewed and prioritized by a Facilities Planning Advisory Committee (FPAC), the members of which include senior executives from a cross-section of NIH. The committee's effort culminates in the development of NIH's Strategic Facilities Plan, which helps shape NIH's Buildings and Space Plan, the Agency Capital Plan, the Federal Capital Improvements Program, and a Five-Year Facility Budgeting Plan.

The B&F program encompasses five major areas that are linked to existing or emerging research needs, regulatory or accreditation guidelines and standards, and/or the unique operating requirements and age of the facilities in NIH's inventory. The five areas are: 1) essential safety and regulatory compliance in lieu of health improvements; 2) new construction; 3) renovations; 4) equipment and systems; and 5) repair and improvements. Under the B&F program, new facilities are programmed for construction or existing facilities are renovated or upgraded on a case-by-case basis, depending on which approach represents the most viable option to support current and emerging research and technological advancements in the NIH intramural research program. The focus of the B&F program is to provide facilities in compliance with applicable safety, accreditation, and other regulatory requirements; efficient in terms of indoor and outdoor environment and energy consumption; and effective in meeting the needs of intramural researchers.

Extramural Assistance. Biomedical research facilities are a critical component of the nation's science and engineering research infrastructure. The availability and condition of biomedical research space directly affects the scope and quality of the biomedical research conducted at the nation's colleges, universities, medical schools, hospitals, and other research organizations. Providing extramural assistance to institutions for the purpose of improving their research capabilities is integral to the success of the NIH extramural research program in achieving its research goals and the national health goals established by DHHS.

The Public Health Service Act (Title IV, Section 481A, *Modernization and Construction of Facilities*) authorizes NIH to "make grants to public and non-profit private entities to expand, remodel, renovate or alter existing research facilities or construct new research facilities" for biomedical and behavioral research and research training. Under the NIH extramural research facilities construction programs, construction grants for extramural research facilities are awarded competitively, with grantee institutions required to obtain matching funds for the specific project awarded. NIH construction grants support the costs of design, renovation, and construction of non-federal basic and clinical research facilities. These grants address the biomedical and behavioral research, research training, or research support needs of an institution or a research area at an institution. Facility construction that may be supported under this program includes construction of new facilities, additions to existing buildings, completion of uninhabitable "shell" space in new or existing buildings, and major alterations and renovations. NIH extramural assistance encompasses "bricks and mortar" modernization as well as total replacement of existing research facilities, providing new capabilities to promote innovative research activity.

To identify current needs for extramural assistance, NIH collaborates with the National Science Foundation in conducting a biennial survey, which is designed to assess the condition of existing facilities nationwide and to identify needs for new and refurbished research facilities. The survey provides the major source of objective data for national research infrastructure policy and planning needs.

GPRA Research Facilities Program					
Budget (dollars in thousands)	**FY 1999 Actual**	**FY 2000 Actual**	**FY 2001 Actual**	**FY 2002 Estimate**	**FY 2003 Request**
	$239,343	**$251,747**	**$248,386**	**$458,677**	**$907,999**

Summary of Performance – Research Facilities Program

Comprehensive summary tables covering all the goals and targets in NIH's Research Facilities Program follow. These tables provide updated information on the status of all of the program's performance targets. More extensive information on each goal, including a chart summarizing the performance results for each target, can be found at the referenced page number.

■ **INTRAMURAL MODERNIZATION AND IMPROVEMENTS**			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
a) Improve the operating conditions and environment of intramural facilities and the availability and reliability of NIH utility distribution systems to support intramural research.	**FY 2003** 1. Complete at least 90% of planned projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities. 2. Complete construction of a Third-Party-Financed 23 megawatts Cogeneration Plant. 3. Begin design to provide a chiller system to support research facilities planned for the south-quadrant of the NIH Bethesda Campus. **FY 2002** Complete at least 90% of planned projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural		Page 257

■ INTRAMURAL MODERNIZATION AND IMPROVEMENTS			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	research facilities. --- **FY 2001** 1. Continue projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities. 2. Complete construction of campus-wide utility distribution systems, renovation and modernization of existing boilers, and extension of the power plant to provide the necessary equipment to support the heating and cooling requirements of facilities on the NIH Bethesda campus. --- **FY 2000** 1. Continue projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities. 2. Complete construction of 90% of planned utility systems for the west and north sections of the campus; complete utility systems supporting the southeast, south, and southwest sections of the campus. **FY 1999** 1. Continue projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural	--- 1. All projects scheduled to correct building and utility system deficiencies were started, and 80% of the scheduled work was completed. All projects scheduled to correct exterior and interior repairs were started, and 86% of the scheduled work was completed. NIH expects to complete the balance of the work by the end of FY 2002. 2. NIH completed construction of the campus-wide utility distribution systems and renovation and modernization of existing boilers. 95% of the power plant extension project was completed. NIH expects to complete construction in FY 2002. --- 1. The balance of the exterior and interior projects was 100 % complete in the second quarter of FY 2001. 2. 100% of the site utilities were completed. 1. The balance of the exterior and interior projects was 100 % complete in the second quarter of FY 2000. The campus utility systems were 100% complete in the third quarter of FY 2000.	

■ INTRAMURAL MODERNIZATION AND IMPROVEMENTS			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	research facilities. 2. Complete construction of the Utility Tunnel Extension Project and the relocation of underground utilities to support the Power Plant Extension Project.	 2. 98% of the Power Plant project was completed in FY 1999 and it was 100% complete in FY 2000. The Utility Tunnel Extension Project was completed as planned.	
b) Complete the Louis Stokes Laboratories Building.	**FY 2001** Complete construction. --- **FY 2000** Complete 95% of the construction. --- **FY 1999** Complete 65% of the construction.	 Construction of the Louis Stokes Laboratories building was completed in FY 2001. --- The 95% construction phase was reached in the first quarter of FY 2001. 90% was completed in FY 2000. --- The 65% phase was reached in the first quarter of FY 2000. 56% was completed in FY 2000.	Page 261
c) Complete the Mark O. Hatfield Clinical Research Center.	**FY 2003** Complete construction of the facility. --- **FY 2002** Complete 75% of the construction. --- **FY 2001** Complete 50% of the construction. --- **FY 2000** Complete the superstructure and exterior wall system. **FY 1999** Complete the design and the first phase of site work.	 --- Construction reached the 50% phase. --- 65% of the superstructure was completed in FY 2000. NIH expects to complete the superstructure and exterior wall system by the end of FY 2002. NIH completed 95% of the scheduled design and 100% of the sitework in FY 1999. The design was completed in FY 2001.	Page 263
d) Complete the Warren Grant Magnuson Clinical	**FY 2003** Start construction of the interim renovations and complete 80% of the	 These targets will be reported on in February 2004 and February	Page 265

■ INTRAMURAL MODERNIZATION AND IMPROVEMENTS			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
Center Revitalization Program.	design effort for Phase I of the Building 10 Renovation Program. --- **FY 2002** Start design for the interim renovations and for Phase I of the Building 10 Revitalization Program.	2003 as appropriate.	
e) Maintain the quality of the NIH Animal Care Program and construct a Central Vivarium/Animal Research Center (ARC).	**FY 2003** Complete 35% of design documents for the facility and 95% of construction documents for sitework and building foundation. **FY 2002** Award a Developer Manager contract for the overall execution of the project and obtain the services of an Architect-Engineering firm to perform the design. **FY 2001** Award a Developer Manager contract, select the design architect-engineering firm, and complete the schematic design. --- **FY 2000** Begin design for the Central Vivarium/ARC site work and foundation, and the programming effort for the facility. --- **FY 1999** Receive accreditation from the Association of Assessment and Accreditation of Laboratory Animal Care International.	To reduce the impact of the FY 2000 delays, award of contracts for a developer manager and an architect-engineering firm will proceed in parallel with the facility programming effort in FY 2002. --- The design began in the summer of 2001. The design will be completed by the fall of 2002 in parallel with the facility programming effort in FY 2002. --- AAALAC accreditation received**.**	Page 267
f) Complete the John Edward Porter Neuroscience Research Center on the NIH Bethesda campus.	**FY 2003** Complete 30% of the construction for this project phase. --- **FY 2002** Start construction of the 200,000 gross square feet facility on the Building 35 site.		Page 270

■ INTRAMURAL MODERNIZATION AND IMPROVEMENTS			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
	FY 2001 Assemble project team and begin demolition of Building 35.	The project team has been assembled and demolition of the facility has begun.	
g) Establish a systematic process to manage and account for NIH's Real Property Inventory.	**FY 2001** 1. Launch a one year pilot program for the Foundation Information for Real Property Management (FIRM) and integrate the lessons-learned into NIH's formalized accounting and reporting procedures for real property management. 2. Validate the NIH real property inventory and populate the FIRM database with the appropriate facility descriptive information, size, function, initial cost, and replacement cost. 3. Provide FIRM online monitoring and reporting capabilities at the desk of each stakeholder involved with real property management.	1. NIH launched the pilot program. Integration of lessons-learned into internal procedures was initiated. 2. All elements of this target have been completed except for the requirement to document replacement cost, which is scheduled for completion in FY 2002. 3. The FIRM software is currently localized and will become a web-based tool that is being developed by the department by the end of FY 2002.	Page 272

■ EXTRAMURAL ASSISTANCE			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
a) Approve an optimal percent of construction designs by the end of the third year that are in compliance with federal and NIH design regulations and guidelines, and with other relevant local, national, and international codes and standards.	**FY 2003** Final construction design documents approved for 75% of grants awarded in FY 2000. --- **FY 2002** Final construction design documents approved for 75% of grants awarded in FY 1999. --- **FY 2001** Final construction design documents approved for: 1. 100% of grants awarded in FY 1998. 2. 50% of grants awarded in FY 1999. 3. 25% of grants awarded in FY 2000. --- **FY 2000** Final construction design documents approved for: 1. 100% of grants awarded in FY 1997.	--- 1. Of the 22 construction awards made in FY 1998, the Division of Engineering Services has approved 20 (91%) construction design documents. The final drawings from the two remaining institutions are expected in FY 2002. 2. Of the 31 construction awards made in FY 1999, the Division of Engineering Services has approved 16 (52%) construction design documents. 3. Of the 45 construction awards made in FY 2000, the Division of Engineering Services approved 10 (22%) construction design documents in FY 2001. During the first month of FY 2002 the Division of Engineering Services approved an additional 2 to make a total of 12 (26%) construction design documents. --- 1. Final construction design documents are expected to be approved for the remaining grant	Page 277

■ EXTRAMURAL ASSISTANCE			
Performance Goals	**FY Targets**	**Actual Performance**	**Details**
		by FY 2002. Final construction design documents have been approved for 96% of grants awarded through FY 2001.	
	2. 50% of grants awarded in FY 1998.	2. Final construction design documents were approved for 77% of grants awarded.	
	3. 25% of grants awarded in FY 1999.	3. Final construction design documents were approved for 23% of grants awarded. By the third quarter of FY 2001, the documents were approved for 40% of grants awarded.	
	----------	----------	
	FY 1999 100% of awarded construction projects meet federal and NIH safety and architectural design regulations and are in compliance with the scope of the application.	The earliest completion date for this target is FY 2003. 83% of awarded projects received final construction design approval by the end of FY 2001.	

2.3.2 Goal-by-Goal Presentation of Performance Goals and Results

2.3.2.1 Intramural Modernization and Improvements

The broad purpose of NIH's Intramural Modernization and Improvements Program (IMIP) is to support the construction, renovation, and maintenance of NIH research facilities located on the Bethesda campus and at off-campus field stations to enable NIH intramural researchers to continue to conduct state-of-the-art medical research. NIH administers the IMIP centrally to benefit all of the ICs' intramural researchers.

To assist the ICs in achieving their research goals, the Buildings and Facilities (B&F) program provides the following support services: 1) ensuring that intramural facilities are in compliance with applicable facility planning, programming, design, construction, environmental, and other regulations to provide safe, functionally adequate, energy efficient facilities in which state-of-the-art biomedical research can be conducted; 2) ensuring that facilities are in compliance with research and accreditation guidelines that can sustain peer reviews and reflect NIH's commitment to excellence as the world leader in biomedical research; 3) enhancing operations and utilization of intramural facilities and the availability and reliability of campus-wide utility distribution systems and supporting equipment; 4) continuing facility renovation, improvement, and new construction projects in response to current and emerging research requirements and technological advancements; and 5) improving the efficiency and effectiveness of the NIH Real Property Inventory.

In addition to these ongoing responsibilities, NIH faces additional challenges due to the age of its facilities, many of which are quite old and have reached or are nearing the end of their useful life. The primary areas of concern are: 1) the inability to continue to provide state-of-the-art research space in aging facilities; 2) the inability to support technological advancements in the current space and its detrimental impact on the recruitment of top researchers and scientists; 3) the escalating maintenance and repair costs associated with the enormous backlog of building deficiencies; and 4) the lack of adequate and reliable sources of power, heating, cooling, communication, security, fire alarm and other utility distribution systems and equipment.

To address these challenges and enhance the IMIP, NIH established seven performance goals:

a) Improve the operating conditions and environment of intramural facilities and the availability and reliability of NIH utility distribution systems to support intramural research.

b) Complete the Louis Stokes Laboratories Building.

c) Complete the Mark O. Hatfield Clinical Research Center.

d) Complete the Warren Grant Magnuson Clinical Center Revitalization Program.

e) Maintain the quality of the NIH Animal Care Program and construct a Central Vivarium/ARC.

f) Complete the John Edward Porter Neuroscience Research Center on the NIH Bethesda campus.

g) Establish a systematic process to manage and account for NIH's Real Property Inventory.

NIH's efforts to achieve these performance goals involve completing the construction of new research buildings on the Bethesda campus, completing construction of new utility systems, reducing the number of deferred projects involving facility repair and maintenance, and designing and implementing a more effective real property management system.

Performance Goal Details - Intramural Modernization and Improvements

Goal a) Improve the operating conditions and environment of intramural facilities and the availability and reliability of NIH utility distribution systems to support intramural research.

NIH's ability to achieve its research goals is impacted greatly by the operating conditions and environment of its intramural facilities. System malfunctions can result in loss of research and delays in the ability to find cures for the world's diseases. As a result, NIH strives to ensure that all modernization and improvements to intramural research facilities keep pace with research and patient care demands, rapidly changing technological advancements, and research priorities. NIH's efforts to improve the reliability and quality of the intramural research environment are focused on two priority areas: 1) reducing the number of deferred projects involving repair and maintenance of NIH facilities; and 2) completing construction of new NIH utility systems on schedule.

NIH's intramural facilities include buildings and utility systems that range in age from 20 to 40 years. Many of these systems are nearing their useful life expectancy. As a result, an extensive backlog of maintenance and repair work (including architectural, structural, mechanical, plumbing, and electrical system repairs) exists.

To systematically reduce the backlog, NIH established procedures to identify, track, monitor, and correct the numerous building deficiencies that impact NIH's ability to achieve its goals. In addition, NIH strives to achieve funding levels for building and infrastructure repairs and improvements consistent with the recommendations of the National Academy of Sciences (NAS). Unless funding is provided at a rate closer to that recommended by the NAS, the backlog of necessary maintenance and repair work will increase, and NIH's ability to meet its research objectives for the 21st century may be impacted.

NIH also installs and maintains large utility distribution systems that provide electricity, steam, and chilled water to campus facilities. A recent achievement in this area includes the completion of the Utility Tunnel Extension Project (i.e., construction of two sections of new underground utility tunnel, totaling approximately 2,000 linear feet, linking to existing tunnels). Planned utility system projects include the construction of a cogeneration plant and the design of a chiller system to support research facilities planned for the south quadrant of the NIH Bethesda campus.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Reduce the number of deferred projects involving repair and maintenance of NIH facilities:					
Continue projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities.	◇→	◆			
Continue projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities.		◇→	◆		
Continue projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities.			◇→	◇	
Complete at least 90% of planned projects to correct building and utility system deficiencies and to improve the interior and exterior of buildings and off-campus facilities consistent with standard industry practices and as necessary to ensure safe and efficient operations of NIH intramural research facilities.				◇	◇
Complete construction of new NIH utility systems on schedule:					
Complete construction of the Utility Tunnel Extension Project and the relocation of underground utilities to support the Power Plant Expansion Project.	◇→	◆			
Complete construction of 90% of planned utility systems for the west and north sections of the campus; complete utility systems supporting the southeast, south, and southwest sections of the campus.		◆			
Complete construction of campus-wide utility distribution systems, renovation and modernization of existing boilers, and extension of the power plant to provide the necessary equipment to support the heating and cooling requirements of facilities on the NIH Bethesda campus.			◇→	◇	
Complete construction of a Third-Party-Financed 23 megawatts Cogeneration Plant.					◇
Begin design to provide a chiller system to support research facilities planned for the south-quadrant of the NIH Bethesda campus.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH made progress in reducing the number of deferred projects involving the repair and maintenance of its facilities.** In FY 1999, NIH completed all but 8% of the exterior and interior repairs and all but 14% of the campus utility systems projects that were part of the backlog. The balance of this work was completed in February 2000 and June 2000, respectively. In FY 2000, NIH completed all but 7% of the interior and exterior building systems projects that were in the backlog, and the balance of the work was completed in February 2001.

Substantial progress in reducing the number of deferred projects was made in FY 2001, as shown in the table below. Specifically, 100% of the roof repairs and off-campus facility repair were completed on schedule. Due to funding constraints, however, only 80% of the projects to correct building and utility system deficiencies and only 86% of the exterior and interior repair projects were completed by the end of the fiscal year; the balance of the work in these categories is expected to be completed in the third quarter of FY 2002.

FY 2001 Assessment Summary
for Improving the Maintenance of NIH Intramural Facilities

Backlogged Area	Scheduled Projects	Completed Projects	Projects in Progress	Completion Percentage at end of FY 2001
Campus Utilities	25	20	5	80%
Roof Repairs	6	6	0	100%
Exterior and Interior Repairs	22	19	3	86%
Off-Campus Facility Repairs	4	4	0	100%
TOTAL	57	49	8	86%

- **NIH made substantial progress in constructing new utility systems.** NIH achieved its FY 1999 target to complete construction of the Utility Tunnel Extension Project. NIH also completed 98% of the work required to relocate the underground utilities for the Power Plant Expansion Project by the end of the fiscal year; the balance of the work was completed in FY 2000. In FY 2000, NIH completed 100% of the planned utility system projects required to support buildings in five sections of the NIH campus, exceeding its targeted goal of a 90% completion percentage.

  During FY 2001, construction of the campus-wide utility distribution systems was completed on schedule, and the project to renovate and modernize boilers was completed ahead of schedule. The power plant extension project was 95% complete by the end of the fiscal year; its completion was delayed by unforeseen rock conditions that were encountered during the excavation phase of the project. A revised completion date of January 2002 was set, with no expected impact on the research mission of NIH.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the number and percent of deferred projects that were completed at the end of each fiscal year and the percent of construction completed for each construction project. Process and milestone data were obtained from the Computerized Maintenance Management System (CMMS) and the Project Information Network (PIN) system. The two systems are used to manage and monitor the acquisition, modernization, replacement or

enhancement of NIH's capital assets, incorporating recognized industry standards for organizations that stress efficient and effective project management. Performance data were verified through quality control systems that track, monitor, verify, and validate project goals consistent with internationally recognized standards of operations.

Goal b) Complete the Louis Stokes Laboratories Building.

The Louis Stokes Laboratories (LSL, Building 50) provides laboratories, support spaces, work stations and office space for 650 scientists performing the work of various NIH Institutes and Centers. This six-story, 24,154 gross square meters (260,000 gross square feet) consolidated research laboratory includes specialized areas such as animal facilities, a nuclear magnetic resonation lab, and a cryogenic electron microscope suite. Its state-of-the-art design incorporates such features as generic open labs to foster interaction between researchers, flexible work stations, interstitial space to provide greater adaptive capabilities to changing research requirements, and unique energy saving features.

The Louis Stokes Laboratories support research functions previously housed in various laboratory structures that can no longer meet the needs of today's research and technological advancements. The consolidated laboratory provides an environment where collaborative research can take place and potentially result in faster delivery of cures for infectious diseases and disorders. Various NIH ICs plan to use this facility, including the National Institute of Diabetes and Digestive and Kidney Diseases, National Human Genome Research Institute, National Cancer Institute, National Institute of Allergy and Infectious Diseases, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institute on Deafness and Other Communication Disorders, and National Heart Lung and Blood Institute.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Complete 65% of the construction.	◇→◆				
Complete 95% of the construction.		◇→◆			
Complete construction.			◆		

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH completed construction of the Stokes Laboratories building on schedule.** By the end of FY 1999, NIH had completed 56.4% of the construction, somewhat less than the 65% target. Delays were primarily due to the need to make space adjustments to support current and projected research requirements. The balance of this work was completed in December 1999. By the end of FY 2000, NIH had completed 90% of the construction, which was close to its 95% target. NIH met this target in the first quarter of FY 2001. NIH met its long-term goal to complete construction of the Louis Stokes Laboratories building in FY 2001.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the percent of construction completed at the end of each fiscal year. Process and milestone data were obtained from the CMMS and PIN systems. Performance data were verified through quality control systems that track, monitor, verify, and validate project goals consistent with internationally recognized standards of operations.

Goal c) Complete the Mark O. Hatfield Clinical Research Center.

The Mark O. Hatfield Clinical Research Center (CRC) will provide 78,965 gross square meters (850,000 gross square feet) for a 250-bed research hospital, allied clinical facilities, and adjacent laboratories. The CRC will become the new heart of the intramural research program, where cutting edge clinical research can transfer basic science discoveries into clinical applications that address many of the DHHS national health goals described in the Healthy People 2010 initiative and the strategic research goals of each NIH Institute and Center.

A congressional review of the importance of NIH's intramural research program and the vital role that clinical research plays in the success of its mission revealed the need for a new clinical research center. An analysis of the condition and the adequacy of the existing Warren Grant Magnuson Clinical Center (WGMCC) indicated that the CRC should be located near the WGMCC to provide an opportunity for appropriate, adaptive reuse of the existing structure. As a result, NIH has undertaken steps to complete construction of the CRC by FY 2003. The photo below shows the new CRC under construction.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Complete the design and first phase of site work.	◇→	→	◆		
Complete the superstructure and exterior wall system.		◇→	→	◇	
Complete 50% of the construction.			◆		
Complete 75% of the construction.				◇	
Complete construction of the facility.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **Construction of the Hatfield Clinical Research Center moves forward.** During FY 1999, NIH completed the first phase of the site work on schedule (in January 1999) and nearly completed the building design on schedule, with 95% of the work achieved by the end of the fiscal year. NIH completed the design in FY 2001, following finalization of programmatic issues involving the optimal use of space.

  During FY 2000, the construction project progressed on schedule until NIH encountered unforeseen conditions during placement of the utility distribution systems on the site. As a result, NIH completed only 65% of the superstructure by the end of FY 2000. Because construction of the exterior wall system depends on completion of the superstructure, its construction had to be delayed. In FY 2001, NIH successfully met its target to complete 50% of the construction.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the completion of the design work, superstructure, and exterior wall system for the CRC, and the percent of construction completed. Process and milestone data were obtained from the CMMS and PIN systems. Performance data were verified through quality control systems that track, monitor, verify, and validate project goals consistent with internationally recognized standards of operations.

Goal d) Complete the Warren Grant Magnuson Clinical Center Revitalization Program.

NIH is renovating and revitalizing the Warren Grant Magnuson Clinical Center (WGMCC, Building 10) for adaptive reuse to support NIH's research mission. This project will reconfigure space in the existing facility to reduce over-crowded conditions, satisfy emerging research initiatives that can no longer be accommodated within the existing facility, and address congressional mandates. NIH will replace building systems to provide adequate capacities, to mitigate potentially unsafe environmental conditions, to reduce maintenance and operating costs, and to allow for research programs to thrive within the Clinical Center complex.

This revitalization is possible because construction of the new Mark O. Hatfield Clinical Research Center (CRC) will provide clinical center functions without disruption. Therefore, NIH has a unique opportunity to revitalize Building 10 while maintaining a clinical environment to facilitate achievement of the DHHS national health goals.

Building 10 has undergone numerous renovations and expansions in the past. Studies indicate that the major building systems providing critical electrical power, lighting, heating, ventilation, air conditioning, and plumbing services in Building 10 vary in age and condition, do not have the capacity to meet the current demands of research, and are at the end of their service life. As a result, routine maintenance and system repairs cannot keep pace with the vast number of deficiencies and operating inefficiencies in the facility.

A primary objective of NIH is to complete the renovation of Building 10 on schedule. Success of the Building 10 Revitalization Program depends on completing the interim construction efforts on various floors of the facility. This interim construction will provide space for administrative and laboratory programs that will remain in Building 10 after the CRC is completed. Without this action, NIH will not be able to provide safe, efficient, and code compliant space for programs not included in the new CRC and programs that are integral to and support the Building 10 Revitalization Program. Phase I of the Building 10 Revitalization Program can begin once NIH completes the interim renovations.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Start design for the interim renovations and for Phase I of the Building 10 Revitalization Program.				◇	
Start construction of the interim renovations and complete 80% of the design effort for Phase I of the Building 10 Renovation Program.					◇

◆ Target Met | ◇ Target Active | ◇⟶ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

NIH established this goal in FY 2001. Therefore, no performance has been reported to date. Initial reporting will begin in February 2003.

Verification/Validation of Performance Measures and Data Issues

Performance will be measured by the initiation of the design for both the interim renovations and Phase I of the Building 10 Revitalization Program, by the initiation of construction of the interim renovations, and by the percent of the design effort completed for Phase I. Process and milestone data will be obtained from the CMMS and PIN systems. Performance data will be verified through quality control systems that track, monitor, verify, and validate project goals consistent with internationally recognized standards of operations.

Goal e) Maintain the quality of the NIH Animal Care Program and construct a Central Vivarium.

NIH is committed to building a modern, compact, and state-of-the-art Central Vivarium/Animal Research Center (ARC) to replace its aging animal facilities. This new central facility will maintain the quality of the NIH animal care program by consolidating ongoing animal programs into an efficient, effective, and well-functioning space to respond to current and emerging research needs for animal modeling.

The existing animal facility complex, located in Buildings 14/28, houses various animal species to support the research requirements for the NIH Institutes and Centers on the Bethesda campus. The sprawling nature of the complex, aging structures (both over 40 years old), deteriorating facility conditions, limited capabilities of the infrastructure, and other limitations imposed by the outdated design, have driven the need for significant renovations and upgrades.

For the intramural research program to fulfill its mission, it is essential that NIH maintain the quality of its animal care program and that its animal care facilities meet the high standards for accreditation set by the Association of Assessment and Accreditation of Laboratory Animal Care International (AAALAC). It is also crucial that the condition and environment of each facility be suitable and adaptable to emerging research demands. Construction will provide central utilities; site work animal holding, receiving, and quarantine areas; procedure rooms; specialized laboratories; administrative support spaces; and the necessary mechanical, electrical, and other utility systems needed to comply with AAALAC accreditation guidelines and other applicable building codes and regulations.

To ensure the continuing effectiveness of the animal care program, NIH has focused its efforts on 1) maintaining high quality animal care facilities for the NIH intramural research program; and 2) completing the construction of the Central Vivarium/ARC on schedule.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Maintain high quality animal care facilities for the NIH intramural research program:					
Receive accreditation from the Association of Assessment and Accreditation of Laboratory Animal Care International.	◆				
Complete construction of the Central Vivarium/Animal Research Center on schedule:					
Begin design for the Central Vivarium site work and foundation, and the programming effort for the facility.		◇→	→	◇	
Award a Developer Manager contract, select the design architect-engineering firm, and complete the schematic design.			◇→	◇	
Award a Developer Manager contract for the overall execution of the project and obtain the services of an Architect-Engineering firm to perform the design.				◇	
Complete 35% of design documents for the facility and 95% of construction documents for sitework and building foundation.					◇

◆ Target Met	◇ Target Active	◇→ Target Not Met and Extended	✖ Target Not Met

Summary of Performance Results

- **NIH maintains high quality animal care facilities for the intramural research program.** NIH met the FY 1999 target to receive accreditation from AAALAC on schedule. AAALAC surveyors conducted a site visit during the week of July 26, 1999. NIH received confirmation of "Deferred Continued" AAALAC accreditation based on the recommendations of the site visit team.

- **Construction of the Central Vivarium/ARC has been delayed.** NIH partially achieved the FY 2000 target to begin the facility programming effort, with discussions underway at the end of the fiscal year. However, before commencing with design work, NIH administrators felt it was prudent to examine, in concert with the update of the Bethesda campus master plan, which programs and functions would be optimal for placement in the ARC. Facility programming discussions, planning activities, and analyses were conducted to ensure that the facility would support NIH's science mission, complement future development in the south quadrant of the campus, meet NIH's strategic animal research needs, and reflect newly emerging animal research modeling requirements.

  To reduce the impact of the FY 2000 delays, NIH made adjustments to the FY 2001 and 2002 targets so that the awarding of contracts for a developer manager and an architect-engineering firm could proceed in parallel with the facility programming effort. Because the design and construction phases of the Central Vivarium depend on the completion of the programming phase, the new strategy called for beginning the design for the sitework in the 1st quarter of FY2003 (December 2002), completing the design for this phase by the 2nd

quarter FY2004 (February 2004), and starting construction by the 4th quarter of FY2004 (July 2004). Completion of the construction for the ARC is targeted for the end of FY 2007, with commissioning and occupancy to be completed in the second quarter of FY 2008.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by the receipt of AAALAC accreditation, initiation of the design for the Central Vivarium/ARC, and awarding of contracts. Process and milestone data were obtained from the CMMS and PIN systems. Performance data were verified through quality control systems that track, monitor, verify, and validate project goals consistent with internationally recognized standards of operations.

Goal f) Complete the John Edward Porter Neuroscience Research Center on the NIH Bethesda campus.

The John Edward Porter Neuroscience Research Center (NRC) on the Bethesda campus will provide a collaborative environment for state-of-the-art neuroscience research with biomedical research laboratories, research support, a vivarium (for both small animals and primates), lab offices, conference facilities, a cafeteria, interaction areas, and shared public spaces. When completed, the NRC will be a multi-level facility with approximately 55,740 gross square meters (600,000 gross square feet), designed and constructed to be sensitive to the site and the adjacent structures. The site plan below shows the footprint of the structure.

Creating the NRC is crucial to plans for improving the efficiency and effectiveness of the neuroscience research program at NIH. This goal is very important because nearly all of the space currently housing NIH neuroscience programs is unsuitable by today's research standards. During the past 30 years, NIH was unable to renew buildings that house neuroscience research and, as a result, the facilities available to NIH neuroscientists did not keep pace with technological breakthroughs in genetics and imaging.

In addition to using outdated facilities, the neuroscience program at NIH is dispersed among several ICs. Scientists are segregated in one or more preclinical departments and removed from colleagues in the clinical departments of neurology, psychiatry, neurosurgery, or anesthesiology. Furthermore, NIH conducts most of its cellular and molecular neuroscience in Building 36, where most of the laboratories in the facility are partitioned into small modules, separated by concrete walls. Eliminating these artificial barriers would create an environment where scientists could focus more intently on fundamental and clinical research, collaborate more productively, and translate their scientific findings more quickly into effective therapies for neurological and psychiatric disorders.

Completing construction of the NRC efficiently and on schedule requires a phased approach. The initial phase includes demolishing an existing older building (Building 35) and constructing the first 18,580 gross square meters (200,000 gross square feet) of the NRC. The neuroscience research program housed in Building 36 will then be relocated into this new facility. Building 36 will then be demolished and the remaining 37,160 gross square meters (400,000 gross square feet) of the NRC will be constructed.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Assemble project team and begin demolition of Building 35.			◆		
Start construction of the 200,000 gross square feet facility on the Building 35 site.				◇	
Complete 30% of the construction for this project phase.					◇

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **Construction of the Porter Neuroscience Research Center is on schedule.** The project team responsible for overseeing the construction of the NRC was established and met during FY 2001, and the demolition of Building 35 was begun on schedule.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by evidence that the project team had assembled and the demolition of Building 35 demolition had been initiated. Process and milestone data were obtained from the CMMS and PIN systems. Performance data were verified through quality control systems that track, monitor, verify, and validate project goals consistent with internationally recognized standards of operations.

Goal g) Establish a systematic process to manage and account for NIH's Real Property Inventory.

NIH has more than 200 buildings in its real property inventory, devoting most of this space to scientific research and clinical procedures to support its overall research mission. Managing a real property inventory of this size requires constant oversight and diligent planning with respect to space management, maintenance, repair, and new construction.

Recognizing the need to establish a systematic process to manage and account for NIH's real property inventory, NIH began a one year pilot program in FY 2001 to test and implement the Foundation Information for Real Property Management (FIRM) system. FIRM is a uniformly recognized real property management tool that provides essential accounting and reporting tools to support the overall mission of NIH and to satisfy auditing requirements. NIH plans to use FIRM to track descriptive information, size, function, initial cost, and replacement cost data for all of its facilities.

After the pilot program is completed, NIH will assess FIRM's performance against specific criteria to determine if the management tool met its intended goals. If the pilot is successful, NIH will develop and complete an implementation plan. After the new process has been operating for several months, NIH will verify that the system is operating properly and assess whether its objectives are being met NIH-wide. Eventually, NIH will expand the use of FIRM to give online access to everyone involved with NIH real property management.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Test and implement the Foundation Information for Real Property Management (FIRM) system:					
Launch a one year pilot program for FIRM and integrate the lessons-learned into NIH's formalized accounting and reporting procedures for real property management.			◆		
Validate the NIH real property inventory and populate the FIRM database with the appropriate facility descriptive information, size, function, initial cost and replacement cost.			◇→	◇	
Provide FIRM online monitoring and reporting capabilities at the desk of each stakeholder involved with real property management.			◇→	◇	

◆ Target Met | ◇ Target Active | ◇→ Target Not Met and Extended | ✖ Target Not Met

Summary of Performance Results

- **NIH made progress in testing and implementing the FIRM system.** In FY 2001, NIH successfully launched a one-year pilot program to test and implement the FIRM system. Meetings were held with stakeholders to address weaknesses identified during the pilot that should be corrected, and it is expected that all of the lessons learned during the pilot will be

incorporated into the FIRM management and accounting procedures in FY 2002. NIH also populated the FIRM database in FY 2001 and validated all of the information in the inventory except facility replacement costs, which should be validated in December 2001. At the end of FY 2001, the FIRM software had not yet become a web-based tool; it is expected that all stakeholders involved with real property management will have online monitoring and reporting capabilities at their desk during FY 2002.

Verification/Validation of Performance Measures and Data Issues

Performance was measured by completion of the FIRM pilot program, by a validity assessment of NIH's real property inventory, by the number and percent of facilities entered into the FIRM database, and by the number and percent of stakeholders with FIRM online monitoring and reporting capabilities. Performance data were verified through records maintained by the Office of Research Services regarding the implementation of the pilot program, evaluations conducted by the NIH CFO to assure that this tool is an efficient and effective means for property management at NIH, reports generated from the FIRM system, and lists of individuals who have immediate access to FIRM online monitoring and reporting capabilities.

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2.3.2.2 Extramural Assistance

Biomedical research facilities are a critical component of the nation's science and engineering research infrastructure. The availability and condition of biomedical research space directly affects the scope and quality of the biomedical research conducted at the nation's colleges, universities, medical schools, hospitals, and other research organizations.

NIH's extramural research facilities construction programs work to address this important need for more biomedical research facilities. The broad priorities for these programs are:

- Respond to requests from the extramural research community for financial assistance in undertaking research facility modernization and construction.

- Conduct critical reviews to ensure that the construction of such facilities is safe and appropriately designed to enable the conduct of high quality research.

NIH is authorized under the Public Health Service Act, Title IV, Section 481A "Modernization and Construction of Facilities" to "make grants to public and non-profit private entities to expand, remodel, renovate or alter existing research facilities or construct new research facilities" for biomedical and behavioral research and research training.

Under the NIH extramural research facilities construction programs, construction grants for extramural research facilities support the costs of design, renovation, and construction of non-federal basic and clinical research facilities. These grants address the needs of an institution or a research area at an institution for biomedical and behavioral research, research training, and/or research support. Facility construction that may be supported under this program includes construction of new facilities, additions to existing buildings, completion of uninhabitable "shell" space in new or existing buildings, and major alterations and renovations. This "bricks & mortar" modernization and replacement of existing research facilities provides new capabilities that can open areas to innovative research activity.

NIH collaborates with the National Science Foundation in conducting a biennial survey to assess the condition of existing facilities nationwide and to identify needs for new and refurbished research facilities. The survey provides the major source of objective data for national research infrastructure policy and planning needs. The 1998 survey determined that construction/renovation projects totaling $11.4 billion were needed at scientific and engineering research facilities at colleges and universities but were deferred due to lack of funds. In recognition of these findings, NIH offers funding opportunities on a competitive basis.

The number of extramural research facility construction awards that NIH makes varies from year to year. The number of awards is dependent on the level of funds provided by Congress as well as the number of applications received that are deemed scientifically meritorious. For example, in FY 2000, 44 awards totaling $74.9 million were made, and in FY 1999, 31 awards totaling $29.6 million were made.

Each construction grant application undergoes a two-tiered peer review. First, an NIH scientific and technical peer review group evaluates applications for scientific and technical merit. Next, the National Advisory Council or Board of the Institute or Center conducts a second level of review. Reviewers evaluate applications to determine how the proposed change in the research environment would facilitate the applicant institution's ability to conduct, expand, improve, or maintain biomedical research. It is through this two-tiered peer review process that NIH ensures that awarded construction grants have high scientific and technical merit and meet the changing needs of the research environment.

Applicants must ensure the availability of matching funds for the construction project. Then, when a grant is awarded, NIH must approve the construction designs before construction may begin. The designs are reviewed by engineers at NIH and must meet applicable codes before approval. Review by the engineers, who have expertise in the design of biomedical facilities, also helps to ensure that the facility will be designed in a way that maximally supports biomedical research.

In order to encourage project completion and to review whether the construction is following the approved designs, NIH may conduct site visits during construction and/or after project completion.

Performance Goal Details - Extramural Assistance

Goal a) Approve an optimal percent of construction designs by the end of the third year that are in compliance with federal and NIH design regulations and guidelines, and with other relevant local, national, and international codes and standards.

NIH construction grants for extramural research facilities support the costs of design, renovation, and construction of non-federal basic and clinical research facilities. Although NIH provides funding for these construction projects, it does not have oversight responsibility over a grantee's completion of a construction project. However, if the grantee does not complete the project within the designated timeframe, generally five years, the funds awarded by NIH to the recipient institution revert to the federal government.

The time between award and construction is contingent on the grantee submitting satisfactory designs. Depending on the nature of the project, the grantee may be required to submit up to three sets of designs: schematic, development, and final construction designs. NIH reviews the designs to ensure they are in accordance with federal and NIH design regulations and guidelines, as well as being in accordance with other related local, national, and international codes and standards.

If the grantee does not obtain approval for its final construction designs by the end of the third year, the building may not be completed successfully. Therefore, NIH focuses on ensuring that grantees' final construction designs are reviewed and approved in a timely manner. A third year approval rate of 65% or less is considered unacceptable, 66% to 69% is considered fair, 70% to 74% is considered good, and 75% and above is considered excellent. Previously, NIH also set performance targets regarding the approval of final construction designs in the first and second years of construction, but dropped these targets were dropped after FY 2001 to focus on the third year, which is considered the most significant year for construction grants.

Performance Targets	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003
Ensure that grantees' final construction designs are reviewed and approved in a timely manner:					
100% of awarded construction projects meet federal and NIH safety and architectural design regulations and are in compliance with the scope of the application.					
Final construction design documents approved for 100% of grants awarded in FY 1997.					
Final construction design documents approved for 100% of grants awarded in FY 1998.					
Final construction design documents approved for 75% of grants awarded in FY 1999.					
Final construction design documents approved for 75% of grants awarded in FY 2000.					
Approve 50% of final construction designs by the end of the projects' second year:[1]					
Final construction design documents approved for 50% of grants awarded in FY 1998.					
Final construction design documents approved for 50% of grants awarded in FY 1999.					
Approve 25% of final construction designs by the end of the projects' first year:[1]					
Final construction design documents approved for 25% of grants awarded in FY 1999.					
Final construction design documents approved for 25% of grants awarded in FY 2000.					

[1] The tracking of the percent of final construction designs approved during the projects' first year and second year was discontinued after FY 2001 in order to focus on the third year, which is considered the most significant year for construction grants.

Target Met	Target Active	Target Not Met and Extended	Target Not Met

Summary of Performance Results

- **Progress has been made in ensuring that grantees' final construction designs are reviewed and approved in a timely manner.** For the FY 1999 target, 100% of the construction grants awarded by NIH in the previous three years (FY 1996-1999) received scientific peer review and concurrence, but only 43% received engineering design review and approval of their final construction designs during FY 1999. By the end of FY 2001, 83% had been approved and the 100% target for final construction design approval of these grants was extended until FY 2003. For the FY 2000 target, NIH approved 86% of the final construction design documents for grants awarded three years earlier (in FY 1997), a lower percentage than the 100% target. By the end of FY 2001, 96% had been approved and the 100% target for final construction design approval was extended until FY 2002. For the FY 2001 target, NIH approved 91% of the final construction design documents for grants awarded three years earlier (in FY 1998) and the 100% target was extended until FY 2003. Based on these early results, a more realistic performance target of 85% for approval of final construction design documents was established for FY 2002 and FY 2003.

- **NIH approved more final construction designs by the end of the project's second year than expected.** In FY 2001, 52% of the final construction documents for grants awarded two years earlier (in FY 1999) were approved, a slightly higher percentage than the 50% target.

- **NIH's approval rate of final construction designs by the end of the project's first year nearly met expectations.** In FY 2001, 22% of the final construction documents for grants awarded a year earlier (in FY 2000) were approved. The percentage was slightly lower than the 25% target but by the end of the first month of FY 2002 (October 2001), 26% of the documents had been approved.

Verification/Validation of Performance Measures

Performance will be measured by the issuance of approval letters by the engineers who review the construction designs. Performance data will be verified through these letters, which are maintained as part of the formal record of the official grant files.

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APPENDICES

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Appendix 1

Approach to Performance Assessment

NIH's Annual Performance Plans include both 1) performance goals that can be assessed through objective/quantitative measures and 2) performance goals based on descriptive achievement criteria.

Where objective/quantitative measures can be used, performance assessment is a process, principally, of comparing data on actual achievement with the target levels stated by the Annual Program Performance Plans. The vast majority of NIH's performance goals are of this type.

Where such measures are not available or not useful, GPRA also provides a means for an agency to define performance goals that rely on criteria that are descriptive in nature – through the "Alternative Form" provisions of GPRA (Sec. 1115 (b), P.L. 103-62). This approach is central to the assessment of many of the goals for NIH's research activities.

Further details on the assessment approaches and data sources for each of these types of performance goals are discussed below.

Objective/Quantitative Performance Goals.

As noted above, most of the performance goals in NIH's Annual Plans have objective/quantitative targets. For these goals, data submitted for the assessment process permits a comparison between the actual achievement level and that targeted by the performance goal. In many cases, the performance data are quantitative, drawn from one or more of NIH's databases that support the agency's normal management processes. Or, where the goal is to complete an action or reach an intermediate milestone, data are provided that objectively document the status of the progress.

In FY 2001, we used the following codes in each performance goal chart:

★ **Target Substantially Exceeded** -- Indicates that NIH met certain criteria in addition to those needed to meet the target. An independent Research Assessment Working Group developed the additional criteria on a goal-by-goal basis; they apply only to the qualitative research outcomes goals.

◆ **Target Met or Target Successfully Met** – "Target Met" indicates that NIH's actual performance met or surpassed the stated target for quantitative/objective goals. "Target Successfully Met" applies only to qualitative research outcomes goals. It indicates that NIH met criteria developed by an independent Research Assessment Working Group for that target.

◇ **Target Active** – Indicates when NIH plans to meet the target.

◇→ **Target Not Met and Extended** – Indicates that actual performance fell short of the target and that NIH extended the timeframe for meeting the target.

✖ **Not Met** – Indicates that actual performance fell short of the target and that the target was specific to a particular fiscal year. Therefore, no further action can be taken to achieve the target.

Specifics on the data sources underlying performance assessment vary by the goal – the details are discussed goal-by-goal in Part II of this document. In general, however, the data for assessing objective/quantitative performance goals come from a variety of NIH sources:

Data Tracking and Collection Systems - Most performance comparisons for quantitative goals will be based on data from information systems that are designed to track a particular operation.

For example, the table below identifies some of the data systems that are currently used at NIH to track and develop data for performance comparisons.

System	Purpose	
IMPAC (Information for Management, Planning, Analysis, and Coordination)	IMPAC is a comprehensive database system covering NIH's extramural research activities.	• Records of research contracts • Records of in-process grant applications • Inter- and intra-agency agreements
CRISP (Computer Retrieval of Information on Scientific Projects)	CRISP is a searchable database (maintained by NIH) of federally funded biomedical research projects conducted at universities, hospitals, and other research institutions.	• Abstracts and indexing terms for funded research projects
PRTS (Purchase Request Tracking System)	A comprehensive online data system for NIH managers/administrators to initiate and track purchase requests to vendors.	• Purchase request details • Sources, competition, and purchase order clearance • Delivery status
Edison	Edison supports a "common face" for invention reporting by federal grantees and contractors. (Edison now operates among several Federal agencies, but was pioneered at NIH.) Edison provides technology for NIH (and other federal agencies) to manage extramural invention portfolios in compliance with federally mandated invention reporting requirements.	• Invention disclosures • Patents • Licenses • Invention utilization

Completion of Studies/Actions - Where a goal is to complete an action (e.g., respond to a recommendation), documenting evidence will be provided that confirms the completion or status of the project. Studies and reports developed by and for the use of peer review and advisory councils and other distinguished independent panels and committees are examples of the information useful for this type of GPRA reporting.

Program Evaluation - Objective evaluation studies and analyses are already a well-established component of NIH's regular planning and management activities for its programs. Such studies are used to provide basic data on program performance, identify avenues for program improvement, and consider the implications of emerging issues on program operation. NIH also conducts various special evaluation studies in association with such agencies as the National Academy of Sciences and the National Science Foundation – such as large scale, long-term studies of scientific personnel and training needs, research facilities, and research instrumentation.

Information from ongoing and planned program evaluation studies is used where relevant for GPRA assessment. Some evaluations will be initiated specifically for GPRA assessment purposes.

Assessing Research Outcomes – Descriptive Performance Goals and Independent Review

Agencies whose missions include basic and clinical research face unique challenges in developing the objective/quantitative performance goals preferred under GPRA. NIH has concluded that strictly numeric goals and measures are neither feasible nor sufficient to capture the breadth and impact of NIH's Research Program.

As already noted, the GPRA legislation anticipated the such situations could arise for some agencies and provides the "Alternative Form" approach as a way for an agency to identify performance goals based on criteria which are chiefly descriptive in nature. In such situations, GPRA requires an agency to develop an assessment process that is *systematic* and *independent* and can provide *objective evaluation* of the agency's achievements relative to the stated performance goals.

For NIH, this approach applies to five of its seven Research Program outcome goals:

Goal A: Add to the body of knowledge about normal and abnormal biological functions.

Goal B: Develop new or improved instruments and technologies for use in research and medicine.

Goal C: Develop new or improved approaches for preventing or delaying the onset or progression of disease and disability.

Goal D: Develop new or improved methods for diagnosing disease and disability.

Goal E: Develop new or improved approaches for treating disease and disability.

The Challenge of Measuring Research Performance. Conventional scientific research metrics (e.g., publications, citations, and patents) gauge only some dimensions of research output. These measures provide relevant data, but they are insufficient for generating a full picture of the progress and outcomes of a research program.

As the President's Office of Science and Technology Policy (OSTP) and the numerous others who have studied the processes of science, technology, and innovation over many years have commented, the linkages between inputs and outputs in science are complex and non-linear:

- Outcomes are usually very difficult to foresee with any degree of accuracy.

- The full value of any given research finding is usually only barely visible at the time of discovery, and reaches a state of fruition often only after many years or in combination with other advances.

- Furthermore, the downstream impact of basic research is usually dependent on substantial further development of new knowledge by private industry, other public sector researchers, or other economic actors.

Scientific advances are generally incremental, building upon previous discoveries. The importance of a particular discovery may not be apparent immediately. Its significance and impact upon human health and quality of life may become evident only after years of continued research.

Accordingly, any assessment process looking at research performance must recognize these difficulties and strive to present an analysis that accounts for the full picture of accomplishment.

Intermediate vs. Ultimate Outcomes. The ultimate outcomes of medical research are, of course, improved health, longevity, and quality of life for all Americans. Each year the NIH can document a number of major medical "culminations" that are visible as practical health benefits, and are often accompanied by economic benefits.

In the recent past, for example, NIH-supported research culminated in the first successful treatment for acute ischemic stroke, using recombinant tissue plasminogen activator (tPA). It has also contributed to the declining mortality rates for many cancers, including some common ones, and to a reduction in disability rates among the elderly. Additionally, while we do not yet know exactly how the human immunodeficiency virus (HIV) causes AIDS, we have learned enough crucial information about HIV to develop effective therapies for patients with AIDS.

The results of efforts by government, academic, and industry scientists are the drug combinations that have markedly improved and extended the lives of many people infected by the HIV.

Nevertheless, the more numerous and immediate outcomes of the Nation's investment in medical research are the incremental findings and accomplishments that increase our knowledge of fundamental life processes. These "intermediate" advances or "inspirations" provide building blocks for future medical culminations.

For example, a detailed map of portions of the human genome was recently assembled and posted on the Internet. This easily accessible map provides the latest research information about genes and their function in both health and disease in a well-organized and easily understandable manner. It provides scientists and medical personnel, as well as students and the public with a window of progress on one of the most extraordinary scientific undertakings of our century—the mapping of the human genome. The mapping project has already advanced our understanding of the genetic basis of many diseases by significantly accelerating a number of disease gene hunts. The map was instrumental, for instance, in locating and isolating genes responsible for Alzheimer's disease, inherited colon cancer, a bone growth disorder resulting in short stature, and a congenital digestive disorder.

None of these intermediate accomplishments directly and/or immediately improve human health. They are, however, essential research steps that enable further work that will lead to improved understanding, diagnosis, treatment, and prevention of human disease and are the expected outcomes of NIH's mission.

Independent Review Process. In response to the requirements of GPRA, NIH has developed an approach for annually assessing the outcomes of its research outcomes that provides an independent and objective account of the agency's science achievements relative to the Research Program's stated performance goals. In brief, an independent review group, impaneled by NIH, examines current information provided by the agency on its recent research achievements and gauges the extent to which NIH research has yielded important discoveries, new knowledge, and improved technologies that can be applied to the development of new or improved diagnostics, treatments, and preventive measures.

This review and evaluation is conducted by a working group of the Advisory Committee to the Director (ACD), NIH. The Assessment Working Group is composed of members of the ACD, the Director's Council of Public Representatives (COPR), and members of Institute and Center national advisory councils.

Sources of Data for the Independent Review Process. The principal data inputs to the Assessment Working Group's review/evaluation process are narrative information that document and characterize significant research accomplishments that have recently resulted from NIH conducted or funded research. These narratives place a specific research advance within the context of what was previously known and unknown about the topic; the scientific and/or medical significance of the research area and the accomplishment; potential applications of

knowledge from the research, if known; and potential economic implications of the advance, if known. This information provides perspective for where an advance fits in within the continuum of medical research, and its potential or direct contribution to understanding and improving human health.

This narrative information is of four principal types:

- *Science Advances*. Describe a specific scientific discovery published within the past year and supported by NIH funding, places it in the larger context of what is known and unknown and describes the significance of the finding to science, health, and/or the economy. Science advances are one-page narratives that contain a descriptive title, a background section, a description of the advance, a discussion of the significance or implications of the advance, and citations of the scientific publications that support the advance. The actual published articles were not provided as part of the assessment materials, but were provided upon request and at the Working Group meeting.

- *Science Capsules*. Provide a snapshot of the breadth and scope of NIH Research Program outcomes. There are obvious limitations to the sheer number of detailed, one-page science advances that the Working Group members could be expected to review and assimilate. Science capsules, consist of a short paragraph that succinctly describes an advance and its significance, as well as citations.

- *Stories of Discovery*. Address the major limitation of traditional science advances–the fact that they address a single, incremental finding. Biomedical progress is usually achieved through long-range investments in research; advances usually occur slowly and incrementally, typically build upon one another, and sometimes have applications to seemingly unrelated areas of medicine. Stories of discovery are 1-2 page narratives that focus on one topic. Each story traces the major developments in that area over several decades. Important connections between advances in science and improvements in the quality of life, health, and health care, as well as any resulting economic benefits are also highlighted.

- *Research Awards/Honors*. Demonstrate outside evaluation and recognition of the value of NIH Research Program outcomes. The award write-ups are brief descriptions of national and international scientific awards/honors received by NIH scientists and grantees within FY99. The brief narratives identify the researcher(s) and the award, describe the work being honored, and the significance/purpose of the award.

Together, these kinds of information provide an extensive, but by no means exhaustive, illustration of NIH's research outcomes, which directly address the Research Program's performance goals.

Data Validation and Verification

Most of NIH's performance goals contain quantitative or otherwise objective targets. Accordingly, in most cases, the basis for performance assessment involves data that are uncontroversial, credible, and open to independent public scrutiny (e.g., material readily available through NIH's website).

For any given goal, the strengths and limitations of the data sources used in preparing the annual performance assessment can vary. These issues are reviewed, as they arise, in the *Performance Assessment Approach* discussion that accompanies each performance goal in Part II. Where there are any issues about the nature and completeness of a data series for a particular evaluation task, they are identified in the course of this discussion.

NIH has established and maintains a number of large-scale databases to meet its ongoing management needs (such as IMPAC – see the earlier discussion above) or with other federal agencies (such as Edison – see earlier above). These databases play a role in the agency's GPRA performance assessment process. In general, these are public databases, created over a number of years through competitive proposals and subject to outside review by knowledgeable experts, and are maintained through standard database quality protocols. These data are widely regarded, within and outside of NIH, as providing a credible picture of various aspects of the nation's biomedical research enterprise.

The "Alternative Form" assessment approach used for the research outcome goals poses some unique issues for data validation and verification. Nonetheless, virtually all of the outside advisory groups that have looked at this issue over the last several years (e.g., the White House Office of Science and Technology Policy, National Academy of Sciences panels and committees, the Office of Naval Research, and various other science agencies) have affirmed the centrality of peer review by technical experts in preparing findings about the productivity of basic research programs. (See, for example, the National Academy of Science's 1999 report *Evaluating Federal Research Programs: Research and the Government Performance and Results Act*.)

As discussed earlier, the approach NIH uses to prepare these annual assessments of its research goals relies chiefly on such a peer review process. The review committee includes individuals outside of NIH with appropriate expertise, to assure both objectivity and sound findings.

Finally, performance assessment for some goals can involve completion of special program evaluation studies. Such work is often conducted at NIH through outside contractors, who can bring particular expertise to bear on the analytical issues at hand. Contracts for such efforts are typically awarded through competitive proposals and subject to technical review, both prior to contract award and later, with draft final report in hand.

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Appendix 2

Changes and Improvements Over Previous Year

NIH's FY 2003 Annual Plan retains the essential features of the documents submitted in the previous fiscal years. This includes organization of the agency's activities into three aggregated (trans-NIH) Core Programs, including Research, Research Training & Career Development, and Research Facilities. It also includes performance goals that address both program outcomes and the means (processes) by which NIH's programs are implemented. The material is presented in the standardized format specified by the DHHS for all OPDIV Annual Plans/Reports.

While retaining the overall DHHS format, significant changes and improvements were made in FY 2003 plan to provide and communicate the performance information more clearly, reduce redundancy where possible, and focus the performance story on the multiple year history and plans for each goal. Key changes include the following:

Consolidation of Performance Goals Summary Tables. The Performance Goals Summary Tables for each section were combined and placed at the beginning of each program. This change provides the reader with a consolidated source for all the performance information for each program.

Updating of performance target information in Performance Goals Summary Tables. Performance information was updated in the Performance Goals Summary table through December 31, 2001 for all current goals where actual performance did not meet planned target levels in previous years.

Elimination of redundant targets. Where goals had redundant targets as a result of a previous FY target not being met, the redundant target was eliminated. The original target is listed as "Target Not Met and Extended" and will be reported on each FY. It will be identified as met in the FY it is met.

Modification of information provided under Performance Goal Details. To better convey the importance of each goal and to provide enhanced information regarding NIH's progress toward the goal and the status of the goal achievement, the following significant modifications were made to the Performance Goal Details for each goal:

- The supporting information, including the goal background and information on the data to support the goal, was strengthened.

- Performance charts that group targets by the major activities NIH undertakes to achieve each goal were added. These charts assist the reader in understanding the multiple dimensions in goal achievement, demonstrate graphically how well NIH is performing

within each activity, identify past targets that were not met and when they are expected to be met (if applicable), and indicate future targets. The legend for these charts is explained in Appendix 1.

The Summary of Performance Results was modified to provide a multiple-year summary of goal performance from inception through the reporting year, rather than a single-year snapshot. This summary parallels the performance chart.

Summary of Goal Status – FY 1999 to FY 2003

A summary of goal status for FY 1999 through FY 2003 is provided in the table below. This summary represents the status of FY 1999, FY 2000, and FY 2001 targets at the end of each targeted FY and as of December 31, 2001. This summary is provided only as a descriptive indicator of the status of our targets from one year to the next. Because goals and targets vary with regard to degree of importance to the NIH mission, summary data does not accurately reflect NIH's overall success.

Fiscal Year		Targets	Level of Achievement							
			Program	Number of Targets	End of Targeted FY			As of December 31, 2001		
						Extended	Not Met	Met	Extended	Not Met
1999*	46	86	Research (36)	62	55	5	2	60	0	2
			Training (4)	16	10	4	2	12	2	2
			Facilities (6)	8	3	5	0	7	1	0
2000	44	88	Research (32)	65	49	14	2	59	3	3
			Training (6)	14	6	5	3	7	4	3
			Facilities (6)	9	3	6	0	6	3	0
2001	36	90	Research (23)	63	52	9	2	53	8	2
			Training (6)	15	10	4	1	10	4	1
			Facilities (7)	12	5	7	0	6	6	0
2002	36	82	Research (24)	61	To be reported in February 2003.					
			Training (6)	15						
			Facilities (6)	6						
2003	35	69	Research (23)	48	To be reported in February 2004.					
			Training (6)	13						
			Facilities (6)	8						

* Notes: Goals that were completed in FY 1999 and FY 2000 were included in this table, but are not reported in this plan. The number of targets that are listed as "Extended" are updated in later plans once the targets are met. The number of targets that are listed as "Not Met" are annual targets whose status will not change.

Goal/Target Changes Over the Prior Year

The table below provides a general appraisal of the changes in this year's Annual Report/Plan.

<table>
<tr><th>Section</th><th>General Appraisal of Goal Changes in the FY 2003 Annual Plan
(for specifics, see the detailed goal statements in Part II)</th></tr>
<tr><td>Research Outcomes

Page 31</td><td>
<table>
<tr><th></th><th colspan="5">Fiscal Year</th></tr>
<tr><th></th><th>1999</th><th>2000</th><th>2001</th><th>2002</th><th>2003</th></tr>
<tr><td>Number of Performance Goals</td><td>7</td><td>7</td><td>7</td><td>6</td><td>6</td></tr>
<tr><td>Number of Targets</td><td>13</td><td>13</td><td>18</td><td>20</td><td>18</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2002 – One fewer goal . Goal e) was combined with goal d) for FY 2002 and beyond.
<u>Goal-by-Goal Comments</u>
▪ Goals a) thorough d) – Sub-goals were added for FY 2002 and beyond.
▪ Goal f) -- One target was split into two targets for more specific reporting for all reporting years.
</td></tr>
</table>

<table>
<tr><th>Section</th><th>General Appraisal of Goal Changes in the FY 2003 Annual Plan
(for specifics, see the detailed goal statements in Part II)</th></tr>
<tr><td>Communication of Results

Page 39</td><td>
<table>
<tr><th></th><th colspan="5">Fiscal Year</th></tr>
<tr><th></th><th>1999</th><th>2000</th><th>2001</th><th>2002</th><th>2003</th></tr>
<tr><td>Number of Performance Goals</td><td>5</td><td>5</td><td>5</td><td>4</td><td>4</td></tr>
<tr><td>Number of Targets</td><td>14</td><td>24</td><td>27</td><td>10</td><td>5</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2002 and FY 2003 – All targets were re-assessed and re-structured in the FY 2003 plan in an effort to produce a more concise, consistent, and informative document. The targets were modified to provide more specific examples of activities to support the goals in this section. Fewer targets are listed as a result which will lead to a more streamlined section.
▪ FY 2002 – One fewer goal planned as a goal is expected to be completed in FY 2001.
▪ FY 2000 – One fewer goal due to merging two goals into one.
<u>Goal-by-Goal Comments</u>
▪ Goal a) -- One FY 2001 target was removed as it was redundant to a FY 2000 target still pending completion. The original target will be reported on. Additionally, one FY 1999 target wqs split into two targets for more specific reporting.
▪ Goal e) -- One FY 2001 target was split into two targets for more specific reporting.
</td></tr>
<tr><td>Technology Transfer

Page 51</td><td>
<table>
<tr><th></th><th colspan="5">Fiscal Year</th></tr>
<tr><th></th><th>1999</th><th>2000</th><th>2001</th><th>2002</th><th>2003</th></tr>
<tr><td>Number of Performance Goals</td><td>3</td><td>3</td><td>3</td><td>3</td><td>2</td></tr>
<tr><td>Number of Targets</td><td>5</td><td>6</td><td>7</td><td>6</td><td>2</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2003 – One fewer goal due to expected goal completion in FY 2002.
</td></tr>
</table>

<table>
<tr><th>Section</th><th>General Appraisal of Goal Changes in the FY 2003 Annual Plan
(for specifics, see the detailed goal statements in Part II)</th></tr>
<tr><td>Research Leadership and Administration

Page 53</td><td>
<table>
<tr><td rowspan="2">Priority Setting</td><td colspan="5">Fiscal Year</td></tr>
<tr><td>1999</td><td>2000</td><td>2001</td><td>2002</td><td>2003</td></tr>
<tr><td>Number of Performance Goals</td><td>3</td><td>2</td><td>1</td><td>0</td><td>0</td></tr>
<tr><td>Number of Targets</td><td>6</td><td>2</td><td>1</td><td>0</td><td>0</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2002 -- This goal is part of the normal research grant selection process and will not be continued past FY 2001.
▪ FY 2001 – One fewer goal due to goal completion in FY 2000.
▪ FY 2000 – One fewer goal due to goal completion in FY 1999 (goal not carried forward in this plan).
</td></tr>
<tr><td>Research Leadership and Administration

Page 54</td><td>
<table>
<tr><td rowspan="2">Grants Administration and Peer Review</td><td colspan="5">Fiscal Year</td></tr>
<tr><td>1999</td><td>2000</td><td>2001</td><td>2002</td><td>2003</td></tr>
<tr><td>Number of Performance Goals</td><td>7</td><td>4</td><td>4</td><td>5</td><td>5</td></tr>
<tr><td>Number of Targets</td><td>8</td><td>7</td><td>7</td><td>7</td><td>6</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2000 – Three fewer goals due to goal completion in FY 1999 (goals not carried forward in this plan). One fewer goal as a result of merging two goals into one.
▪ FY 2001 -- One new goal added.
<u>Goal-by-Goal Comments</u>
Goal a) -- The goal was reworded to be more specific. One FY 2001 target was removed as it was redundant to a FY 2000 target still pending completion. The original target will be reported on.
</td></tr>
</table>

<table>
<tr><th>Section</th><th>General Appraisal of Goal Changes in the FY 2003 Annual Plan
(for specifics, see the detailed goal statements in Part II)</th></tr>
<tr><td>Research Leadership and Administration

Page 58</td><td>
<table>
<tr><td rowspan="2">Agency Management and Administrative Support</td><td colspan="5">Fiscal Year</td></tr>
<tr><td>1999</td><td>2000</td><td>2001</td><td>2002</td><td>2003</td></tr>
<tr><td>Number of Performance Goals</td><td>11</td><td>11</td><td>3</td><td>4</td><td>4</td></tr>
<tr><td>Number of Targets</td><td>16</td><td>13</td><td>3</td><td>15</td><td>14</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2003 – Two new goals (e and f) added
▪ FY 2002 – Two fewer goals planned as the goals are expected to be completed in FY 2001
▪ FY 2001 – Seven fewer goals. Goals deemed not to be “mission critical” were removed from NIH’s GPRA plan after FY 2000. (Many of these goals/targets are tracked for other management reporting purposes, such as for the agency’s Accountability Report.) The significant reduction in the number of goals evident after FY 2000 reflects an intent to include management & administrative matters of only the highest importance in this section.
<u>Goal-by-Goal Comments</u>
▪ Goal a) -- One FY 2001 target was removed as it was redundant to a FY 2000 target still pending completion. The original target will be reported on.
▪ Goal b) -- Targets were added for FY 2002 and FY 2003.
</td></tr>
</table>

<table>
<tr><th>Section</th><th>General Appraisal of Goal Changes in the FY 2003 Annual Plan
(for specifics, see the detailed goal statements in Part II)</th></tr>
<tr><td>Training Support and Outreach

Page 213</td><td>
<table>
<tr><th></th><th colspan="5">Fiscal Year</th></tr>
<tr><th></th><th>1999</th><th>2000</th><th>2001</th><th>2002</th><th>2003</th></tr>
<tr><td>Number of Performance Goals</td><td>4</td><td>6</td><td>6</td><td>6</td><td>6</td></tr>
<tr><td>Number of Targets</td><td>16</td><td>14</td><td>15</td><td>15</td><td>13</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2000 – One new goal was added in FY 2000.
<u>Goal-by-Goal Comments</u>
▪ Goal a) Monitoring the need for new announcements and other outreach activities are routine activities and have been discontinued as explicit targets in FY 2002 and subsequent years. These activities will be described in the narrative.
▪ Goal b) Issuance of announcements is a routine function and has been discontinued as an explicit target for FY 2002 and subsequent years. These activities will be described in the narrative. One target that previously consisted of multiple measures was split into four separate targets for more accurate reporting. This resulted reporting on three additional targets in both FY 1999 and FY 2000.
▪ Goal c) Targets that previously consisted of multiple measures were split into separate targets for more accurate reporting. This resulted in reporting on 2 additional targets for FY 1999 and one for FY 2001.
▪ Goal d) The four targets for FY 2002 replace the previous single target.
▪ Goal e) One FY 2002 target was removed as it was redundant to a FY 2000 target still pending completion. The original target will be reported on.
▪ Goal f) The three targets for FY 2002 replace the previous single target.
</td></tr>
<tr><td>Intramural Modernization and Improvements

Page 248</td><td>
<table>
<tr><th></th><th colspan="5">Fiscal Year</th></tr>
<tr><th></th><th>1999</th><th>2000</th><th>2001</th><th>2002</th><th>2003</th></tr>
<tr><td>Number of Performance Goals</td><td>5</td><td>5</td><td>6</td><td>5</td><td>5</td></tr>
<tr><td>Number of Targets</td><td>7</td><td>6</td><td>9</td><td>5</td><td>7</td></tr>
</table>
<u>Section Comments</u>
▪ FY 2001 – Net increase of one goal. One FY 2000 goal is completed, but two goals are added in FY 2001.
FY 2002 – One fewer goal planned as one goal is expected to be completed in FY 2001.
</td></tr>
</table>

<table>
<tr><th>Section</th><th>General Appraisal of Goal Changes in the FY 2003 Annual Plan
(for specifics, see the detailed goal statements in Part II)</th></tr>
<tr><td>Extramural Assistance

Page 253</td><td>
<table>
<tr><th></th><th colspan="5">Fiscal Year</th></tr>
<tr><th></th><th>1999</th><th>2000</th><th>2001</th><th>2002</th><th>2003</th></tr>
<tr><td>Number of Performance Goals</td><td>1</td><td>1</td><td>1</td><td>1</td><td>1</td></tr>
<tr><td>Number of Targets</td><td>1</td><td>3</td><td>3</td><td>1</td><td>1</td></tr>
</table>
<u>Goal-by-Goal Comments</u>
▪ Goal a) This goal was originally adjusted in FY 2000 and has been course corrected again in FY 2002. The targets for FY 2002 and beyond are based on new baseline data that have been established.
</td></tr>
</table>

Appendix 3

Linkage to DHHS and OPDIV Strategic Plans

NIH's activities (as the other departmental operating divisions) are incorporated in the current Department of Health and Human Service's (DHHS) just released FY 2001-2006 Strategic Plan (published Sept. 2000), as well as in the prior FY 1997-2002 Strategic Plan (published Sept. 1997). NIH's three Core Programs (Research, Research Training and Career Development, and Research Facilities) widely support the six strategic goals and more than three dozen objectives articulated by DHHS in these plans.

The strategic goals and objectives in the current DHHS Strategic Plan (version published Sept. 2000, covering FY 2001-2006) are listed in the table below where there is an NIH role.

NIH's principal linkages arise under *Goal Six: Strengthen the Nation's Health Sciences Research Enterprise and Enhance Its Productivity*, where NIH research is a key element. However, as apparent, NIH's activities also contribute widely to the Department's other goals and objectives.

NIH Involvement With DHHS Strategic Goals/Objectives
Goal 1: Reduce the Major Threats to the Health and Productivity of All Americans
Objective 1.1 Reduce tobacco use, especially among youth
Objective 1.2 Reduce the incidence and impact of injuries and violence in American society
Objective 1.3 Improve the diet and the level of physical activity of Americans
Objective 1.4 Reduce alcohol abuse and prevent underage drinking
Objective 1.5 Reduce the abuse and illicit use of drugs
Objective 1.6 Reduce unsafe sexual behaviors
Objective 1.7 Reduce the incidence and impact of infectious diseases
Objective 1.8 Reduce the impact of environmental factors on human health
Goal 2: Improve the Economic and Social well-being of Individuals, Families and Communities in the United States
Objective 2.3 Improve the healthy development and learning readiness of preschool children

NIH Involvement With DHHS Strategic Goals/Objectives FY 2001-2006 Strategic Plan
Objective 2.5 Increase the proportion of older Americans who stay active and healthy
Objective 2.6 Increase independence and quality of life of person with long-term care needs
Goal 3: Improve Access to Health Services and Ensure the Nation's Health Entitlement and Safety Net Programs
Objective 3.2 Eliminate disparities in health access and outcomes
Objective 3.3 Increase the availability of primary health care services for underserved populations
Objective 3.6 Improve the health status of American Indians and Alaskan Natives
Objective 3.8 Increase the availability and effectiveness of mental health care services
Goal 4: Improve the Quality of Health Care and Human Services
Objective 4.1 Enhance the appropriate use of effective health services
Objective 4.3 Improve consumer and patient protection
Goal 5: Improve the Nation's Public Health Systems
Objective 5.1 Improve the capacity of the public health system to identify and respond to threats to the health of the nation's population
Objective 5.2 Improve the safety of food, drugs, medical devices and biologic products
Goal 6: Strengthen the Nation's Health Science Research Enterprise and Enhance Its Productivity
Objective 6.1 Advance the scientific understanding of normal and abnormal biological functions and behaviors
Objective 6.2 Improve our understanding of how to prevent, diagnose, and treat disease and disability
Objective 6.3 Enhance our understanding of how to improve the quality, effectiveness, utilization, financing, and cost-effectiveness of health services
Objective 6.4 Accelerate private sector development of new drugs, biologic therapies, and medical technology
Objective 6.5 Strengthen and diversity the base of well-qualified health researchers
Objective 6.6 Improve the communication and application of health research results
Objective 6.7 Strengthen mechanisms for ensuring the protection of human subjects in research and the integrity of the research process

References

U.S. Department of Health and Human Services, *Strategic Plan, FY 2001-2006*, September 30, 2000. (See http://aspe.hhs.gov/hhsplan/index.htm)

U.S. Department of Health and Human Services, *Strategic Plan, FY 1997-2002* , September 30, 1997.

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Appendix 4

Performance Measurement Linkages with Budget, Cost Accounting, Information Technology Planning, Capital Planning, and Program Evaluation

Budget

NIH links performance measures to budget and accounting, as appropriate, to meet the requirements of GPRA and other management reporting such as under the Chief Financial Officers (CFO) Act and the Government Management and Reform Act (GMRA).

Under NIH's aggregated approach (see Sec. 1.2), performance goals are grouped according to the three Core Programs: Research, Research Training and Career Development, and Research Facilities. In NIH's current budget and cost accounting system, dollars are not directly associated to each goal (such association is not required under GPRA). However, NIH has developed a "crosswalk" for how each budget mechanism (e.g., Research Project Grant, Research Management and Support, Construction, etc.) links to the core programs. In this way, NIH distributes its total budget authority by GPRA Core Program.

Cost Accounting

NIH develops and reports the cost of its 3 programs on its audited Statement of Net, as required by the CFO Act, the GMRA, and the Office of Management and Budget. These reported costs are derived using an accrual basis of accounting as required by federal accounting standards and the Federal Financial Management Improvement Act. These amounts differ from the reported obligations or budgetary resources included in budget documents that use an obligation basis of accounting.

NIH includes cost measures for performance goals, as appropriate, in its service and supply fund activities. NIH finances these activities using a fee for service cost recovery method. NIH develops cost per unit of good or service and benchmarks these unit costs with other providers of similar or complementary goods and services. Also, NIH strives to increase stakeholder value by reducing the cost per unit of good or service wherever possible.

Information Technology Planning

Information Technology had a discrete set of goals in the NIH GPRA Performance Plan through 2000. These goals, whose accomplishment is summarized below, focused the IT activities of the

agency on the NIH mission and institutionalized a corporate-wide perspective in the management of the IT function. In addition, IT has been woven throughout the NIH research program and linked to goals identified in all three of the Core Programs in the NIH Annual Performance Plan. Although, the IT-specific goals have been accomplished and will be dropped from future Plans, the performance goals that reflect how IT is utilized by the NIH research community will continue to be found in all three of the Core Programs – 1) Research, 2) Research Training and Career Development, and 3) Research Facilities.

The accomplishment of the IT-specific goals began in 1996, when the NIH Director began activities for managing selected elements of IT from a corporate-wide perspective. His first step addressed the organizational structure by hiring a Chief Information Officer (CIO) and the second established the Center for Information Technology (CIT). In addition, two advisory groups were established: the NIH Director formed NIH's IT Board of Governors (BOG), composed of selected senior management from across NIH, and the NIH CIO established the NIH IT Management Committee (ITMC), composed of senior Institute and Center (IC) IT representatives.

Since then, the CIO and its advisory groups have developed a process for managing IT from a corporate-wide perspective to make it more effective in supporting the mission of NIH and in providing integrated systems that support the variety of NIH business processes. They accomplished the following: strengthened the investment review process; established a formal project management structure for enterprise IT; refined and implemented the strategic, corporate "IT vision" for NIH; developed a NIH-wide information security program; and developed interoperability standards.

In addition, guidance was developed to assist the ICs in establishing performance measures and evaluating IT programs based on performance measures, (which can be found at http://www.cit.nih.gov/mgmt-pol.html). Discussions of performance measures were woven throughout the Investment Review process described at http://irm.cit.nih.gov/itmra/invreview.html and were also incorporated in the IT Management Guide, http://irm.cit.nih.gov/itmra/mgtprocess.html. Now, when IC program managers conduct a business case analysis, they are advised to address IT performance measures among others. Resources and tools were made available to facilitate this process and can be found at http://irm.cit.nih.gov/itmra/perfmeasure.html. In addition, the Office of the CIO initiated a recurring class in performance measures, to increase the number of IT and program managers familiar with the creation and use of performance measures.

Having set these organizations, processes, guidelines and tools in place, NIH has focused its Information Technology planning on pursuing the mission of the NIH as described in this Plan. This accomplishment has also enhanced our ability to accomplish the IT-related goals within our Core Programs in conformance with the performance measurement principles of GPRA.

Capital Planning

NIH's planning for capital projects is woven throughout the annual performance plan, notably in the sections addressing "Management and Administration" and "Intramural Modernization and Improvements." Additional information on capital projects can be found in the detailed budget tables prepared by NIH's Office of Financial Management.

Evaluation

Evaluation is the foundation of managing for results. Inevitably, program managers and other decision-makers gather information about a program and make judgments about its worth or value. The quality of those judgments depends on the quality of the information upon which they are based. For that reason, NIH program managers depend on two complementary evaluation activities, *performance measurement* and *program evaluation*, to establish reasonable performance goals and to accurately assess progress toward those goals.

Performance measurement refers to regular monitoring of program accomplishments. Program accomplishments include the activities conducted (process), products produced or services delivered (outputs), and the results of those products and services (outcomes). Performance measurement is conducted by program managers to gauge how well the program is progressing toward its intended goals. The information gained from such on-going tracking systems may alert program managers to emerging problems and may spur a program evaluation to provide more information on why the program is not achieving anticipated results.

Program evaluation refers to systematic investigations or studies that involve assessing the worth and/or performance of particular programs. In most cases, the underlying purpose of a program evaluation is to help program mangers answer specific questions about a program, such as whether it is being implemented as planned or is achieving its intended purpose. Managers typically use the information obtained from program evaluations to understand why certain results are or are not being achieved and to make adjustments in program strategies or activities. NIH conducts four types of program evaluations: needs assessments, feasibility studies, process evaluations, and outcome evaluations. Needs assessments and feasibility studies are usually conducted as preliminary studies (e.g., to improve the design of a more complex process or outcome evaluation). Experts external to the program often conduct program evaluations, but program managers may also conduct them.

Purposes of Program Evaluation Under GPRA

At NIH, program evaluation serves two important purposes under GPRA: to support program planning and to support program performance assessment.

Support Program Planning

Program evaluations provide useful information to NIH's program managers regarding the appropriateness of established performance goals, annual targets, and implementation strategies. For example, needs assessments are typically conducted to identify systematically whom a program is serving and the extent to which their needs are being addressed. They may also explain why certain needs are not being met and how the program could be revised to address the unmet needs. Using the information gained from such evaluations as a foundation for program planning, NIH program managers develop and modify performance goals and targets to more effectively direct their programs toward the desired outcomes. In addition, the strategies used to implement NIH programs are often adjusted based on evaluation findings.

Support Program Performance Assessment

Program evaluations support program performance assessment activities at NIH primarily by providing insight regarding the relationship between NIH activities and the results NIH seeks to achieve. Outcome evaluations are often conducted to obtain methodologically sound information about the effectiveness of a program and to measure the program's progress towards goal achievement. In addition, this information is critical to determining the extent to which a program's activities contributed to any measured progress toward the desired end result or outcome.

NIH managers also use process evaluations to examine program progress (as evidenced primarily by program outputs) and to determine whether programs are being implemented as planned. The information gleaned from these evaluations allows managers to make mid-course corrections and improve program administration. Finally, feasibility studies are used to develop better ways to measure program performance. Examples include developing databases to track information over time, identifying ways to more effectively access existing data sources, developing new data collection instruments, and validating/verifying data sources.

Appendix 5

NIH Institutes and Centers

Institute/Center	Mission
National Cancer Institute	NCI conducts and supports programs to understand the causes of cancer; prevent, detect, diagnose, treat, and control cancer; and disseminate information to the practitioner, researcher, patient, and public. The Institute's efforts are directed at reducing the burden of cancer morbidity and mortality and, ultimately, at preventing the disease.
National Heart, Lung, and Blood Institute	NHLBI's research program is directed at diseases of the heart, blood vessels, lungs, and blood, and at transfusion medicine. Its activities encompass innovative basic, clinical, population-based, and health education research.
National Institute of Dental and Craniofacial Research	NIDCR's research program is directed at understanding, treating, and ultimately preventing the infectious and inherited craniofacial-oral-dental diseases and disorders that compromise millions of human lives.
National Institute of Diabetes and Digestive and Kidney Diseases	NIDDK conducts and supports research, training, health information dissemination, and other programs with respect to diabetes millitus and endocrine and metabolic diseases; digestive diseases and nutritional disorders; and kidney, urologic, and hematologic diseases.
National Institute of Neurological Disorders and Stroke	NINDS conducts and supports research and training on the normal and diseased nervous system to reduce the burden of neurological diseases. The research program is ultimately directed at improving the prevention, diagnosis, and treatment of the hundreds of disorders affecting the nervous system. These include stroke; epilepsy; demyelinating disorders such as multiple sclerosis; tumors; pain; traumatic injury of the brain and spinal cord; degenerative disorders such as Parkinson's disease; movement disorders; developmental disorders such as autism, the myasthenias and muscular dystrophies; and numerous autoimmune, metabolic, and genetic disorders.
National Institute of Allergy and Infectious Diseases	NIAID conducts and supports research that strives to understand, treat, and ultimately prevent the myriad infectious, immunologic, and allergic diseases that threaten millions of human lives.
National Institute of General Medical Sciences	NIGMS supports basic biomedical research that is not targeted to specific diseases, but increases understanding of life processes and lays the foundation for advances in disease diagnosis, treatment, and prevention. NIGMS attempts to ensure the vitality and continued productivity of basic biomedical research, while producing the next generation of scientific breakthroughs and training the next generation of scientists.

Institute/Center	Mission
National Institute of Child Health and Human Development	NICHD conducts and supports research on fertility, pregnancy, growth, development, and medical rehabilitation. The Institute's broad purpose is to ensure that every child is born healthy and wanted, and grows up free from disease and disability.
National Eye Institute	NEI conducts and supports research, training, health information dissemination, and other programs directed at blinding eye diseases, visual disorders, mechanisms of visual function, preservation of sight, and the special health problems and requirements of the blind.
National Institute of Environmental Health Sciences	NIEHS conducts and supports research on how environmental exposures, genetic susceptibility, and age interact to affect an individual's health. Its overall purpose is to reduce the burden of human illness and dysfunction from environmental causes.
National Institute on Aging	NIA conducts and supports research on the biomedical, social, and behavioral aspects of the aging process; the prevention of age-related diseases and disabilities; and the promotion of a better quality of life for all older Americans.
National Institute of Arthritis and Musculoskeletal and Skin Diseases	NIAMS conducts and supports research, training, and information dissemination directed at understanding the normal structure and function of bones, muscles, and skin, as well as the numerous and disparate diseases that affect these tissues.
National Institute on Deafness and Other Communication Disorders	NIDCD conducts and supports basic and clinical research and research training in the normal and disordered processes of hearing, balance, smell, taste, voice, speech, and language. These diseases and disorders currently affect about 46 million Americans. Basic and clinical research focused on understanding the normal processes and disorders of human communication are motivated both by intrinsic scientific interest and importance to the health of the nation.
National Institute of Mental Health	NIMH conducts and supports research on the brain and behavior – basic, clinical, epidemiological, and health services research. The Institute's activities are broadly dedicated to understanding, treating, and preventing mental illnesses.
National Institute on Drug Abuse	NIDA conducts and supports research across a broad range of disciplines that bear on drug abuse and addiction, and disseminates information about its research findings. The Institute's broad purpose is to help reduce drug abuse and to improve the options for addiction prevention and treatment.
National Institute on Alcohol Abuse and Alcoholism	NIAAA conducts research directed at improving the treatment and prevention of alcoholism and alcohol-related problems. The Institute's broad objective is to reduce the enormous health, social, and economic consequences of this disease.

Institute/Center	Mission
National Institute of Nursing Research	NINR has a broad mandate to sponsor research on the clinical care of individuals and their responses to health problems. Scientists supported by the Institute seek to understand and mitigate the effects of acute and chronic illness and disability, promote healthy behaviors and prevent the onset or worsening of disease, and improve the healthcare environment.
National Human Genome Research Institute	NHGRI supports NIH's participation in the Human Genome Project, a worldwide research effort directed at analyzing the structure of human DNA and determining the location of the estimated 100,000 human genes. At the intramural level, NHGRI develops technology for understanding, diagnosing, and treating genetic diseases.
National Institute of Biomedical Imaging and Bioengineering	The NIBIB promotes fundamental discoveries, design and development, and translation of technological capabilities in biomedical imaging and bioengineering, enabled by relevant areas of information science, physics, mathematics, materials science, and computer sciences. NIBIB plans, conducts, fosters, and supports an integrated and coordinated program of research and research training that can be applied to a broad spectrum of biological processes, disorders and diseases and across multiple organ systems.
National Center for Research Resources	NCRR advances biomedical research and improves human health through research projects and shared resources that create, develop, and provide a comprehensive range of human, animal, technological, and other resources. There are four main areas of concentration: biomedical technology, clinical research, comparative medicine, and research infrastructure.
National Center for Complementary and Alternative Medicine	NCCAM conducts and supports basic and applied research and training and disseminates information on complementary and alternative medicine to practitioners and the public.
National Center for Minority Health and Health Disparities	NCMHD serves as the focal point within the National Institutes of Health for planning and coordinating minority health and other health disparities research. The Center coordinates the development of a comprehensive health disparity research agenda that identifies and establishes priorities, budgets, and policy that govern the conduct and support of NIH-sponsored minority health and other health disparities research and training activities.
Fogarty International Center	FIC leads NIH's efforts to advance the health of the American public and citizens of all nations through international cooperation on global health threats.
Warren Grant Magnuson Clinical Center	CC is the clinical research facility of the NIH. It provides patient care, services, training, and the environment in which NIH clinician-scientists creatively translate emerging knowledge into better understanding, detection treatment, and prevention of human diseases.

Institute/Center	Mission
Center for Scientific Review	CSR carries out initial peer review of the majority of research and research training applications submitted to the NIH. Peer review is the foundation of the NIH grant and award process. The Center also serves as the central receipt point for all Public Health Service applications and makes referrals to scientific review groups for scientific and technical merit review and to funding components for potential award.
National Library of Medicine	NLM is one of three national medical libraries. It collects, organizes, and makes available biomedical science information to investigators, educators, and practitioners. It also carries out programs to strengthen medical library services in the United States. NLM's electronic databases, such as MEDLINE, are used extensively throughout the world.
Center for Information Technology	CIT provides, coordinates, and manages information technology and seeks to advance computational science.

Appendix 6

NIH Working Group Assessment Materials

Titles of NIH Research Materials Reviewed by the NIH Research Assessment Working Group

Goal a) Add to the body of knowledge about normal and abnormal biological functions and behavior.

Science Advances

- Heart Muscle Cells Regenerate After a Heart Attack
- Bone Marrow Cells Repair Heart Attack Damage
- Blood Stem Cells Make More than Just Blood
- Research on Rare Disease Provides Insight into How Sterol Consumption Affects Blood Cholesterol Levels
- Understanding of Cholesterol Metabolism Suggests New Line of Therapeutics
- Alzheimer's Genetic Factor is Linked to Sleep Apnea
- Genetic Mutations and Altered Proteins Influence Lymphangioleiomyomatosis
- Link Identified Between Ethnicity and "Asthma Genes"
- Studies Cast New Light on How Pneumonia Develops in AIDS Patients
- Mutation is Associated with Familial Interstitial Lung Disease
- Novel Protein Links Fanconi Anemia with Other Chromosome Instability Syndromes
- Functional Brain Imaging as a Tool to Understand Cochlear Implant Performance
- Exploiting Mouse Models of Disease: Discovery of Novel Deafness Genes and Genetic Interactions that Modify Hearing Impairment
- Hearing Parents of Deaf Children Favor Genetic Testing for Deafness
- An Essential Gene in Development of the Auditory and Vestibular Systems
- The Genetic and Environmental Etiology of Stuttering
- Identification of Genes Causing Deafness in Humans
- Disability Continues to Decline for Older Americans
- Increase in Maximum Age at Death
- Personality Determinants of HIV Risk Perceptions and Behavior Changes
- Persistence of Cognitive Decline After Coronary-artery Bypass Surgery
- More African-Americans than Africans get Alzheimer's Disease
- Regeneration and Tissue Repair: Tapping the Potential of Stem Cells
- Growth Hormone Deficiency Promotes Longevity in Mice
- Structure-function Studies of the Insulin Receptor
- Genetic Alterations Can Cause Increased Life Span in Fruit Flies
- Gene Required for Full Reproductive Lifespan in Women
- BACE1 is the Major Beta-Secretase for Generation of Amyloid-beta Peptides in Mouse Brain
- Molecular Modulators of Memory
- Characteristics of Adult Neural Stem Cells
- Molecular Structure of Key Enzyme Solved
- Designer Mice Eat More, Weigh Less
- Only Two Genes Needed to Form Fish Heads

- Scientists Identify New Chink in a Parasite's Armor
- Hepatitis C Study May Lead to New Treatments
- Genetics of Cancer: Genetic Differences May Reduce Cancer Risk
- Benefits of DNA Replication Errors: How the Immune System Recognizes Invaders
- Combined Studies Show No Association of Exposure to DDE and PCBs with Breast Cancer Risk
- Insight into Molecular Pathways of Asthma
- Arsenic Toxicity
- Maintaining Enzyme Balance for Cellular Defense
- Molecular Insights into Inflammatory Disorders such as Rheumatoid Arthritis and Crohns
- Dietary Deficiencies May Lead to Birth Defects or Childhood Cancer
- A Protein Associated with Memory Loss in Alzheimer's Patients
- Ecstasy Induces Learning and Memory Impairments in Laboratory Animals: Implications for Human Developmental Impairments
- Male Infertility
- Insight into Preventing Damage Caused by Balloon Angioplasty and Other Procedures
- New Insights into the Development of Arthritis
- Pathogenic Mechanism in a Novel Limb-Girdle Muscular Dystrophy
- Role of Angiogenesis Hormone in Skeletal Muscle Hypertrophy
- Molecular Causes of Painful Joints in Juvenile Rheumatoid Arthritis
- New Insights into the Complex Effects of Estrogen on Bone
- Association of COMT Genotype and Risk for Schizophrenia
- Neuronal Synchronization
- Specifying the Brain Structures Involved in Acute Fear versus Anxious Temperament
- Brain Changes in Childhood Schizophrenia
- His 'n' Her Brains: Molecular Designs for Sexual Differentiation
- Imaging Glucose Metabolism to Streamline Treatment Efficacy Research in Alzheimer's
- Deciphering Brain Molecules Responsible for Learning and Expressing Fear
- Adjusting Receptor Numbers at Synapses
- Neurogenesis: New Memories Require New Cells
- Synaptic Vesicle Protein 2 (SV2) as a Key Regulator of Neurosecretion
- Identification of a Potential Vulnerability Gene for Autism
- Cytoskeletal Defect Causes Alexander Disease
- How Huntington's Disease Kills Brain Cells
- Genetic Findings Lead to Clues about Parkinson's Disease
- Understanding How Trauma Damages Brain Cells
- Mathematical Model Enables Estimation of Cost-Effectiveness of HIV/AIDS Treatment
- Gene Variant is Associated with Reduced Risk for Heart Attack
- Scientists Elucidate Structure of Mysterious Pathogen-Reacting Protein
- New Model for Hepatitis C Virus Replication will Advance Basic Research and Drug Development
- Amyloid-β and Implications for the Alzheimer's Disease Process
- "Front Line" Immune Cells Have a Surface Protein that is Critical for Responding to a Specific Virus
- Scientists Identify Gene Activated by Vaccine Enhancers
- Researchers Identify Immune Cells that Help Transmit HIV Throughout the Body
- Regulating the Development of the *Leishmania* Parasite's Infective Stage
- Drugs, Food, and Gambling: Is there a Commonality?
- MDMA Use During Pregnancy Can Impair Memory and Learning in Offspring
- Despite Lower Initial HIV Blood Levels in Women Men and Women Develop AIDS at Similar Rates
- Key Transcription Factor May Play Role in Transition from Voluntary Cocaine Use to Addiction
- Even a Single Exposure to Cocaine Can Alter Brain Function
- Progress Made in Understanding the

Neurobiological Basis of Relapse and the Role that Memory Plays
- A Person's Craving for Drugs Can Override All Other Motivational Priorities
- Structure of a Gene Expression Machine
- Microarray Analysis of Gene Expression in a Worm
- Detection of Mutations in Transgenic Fish
- A Promising Gene Therapy Vector
- A Comparative Map of the Zebrafish Genome
- New Methods for Analysis of Protein Phosphorylation
- Transgenic Expression in Rhesus Monkey Placental Tissues
- Cancer Virus Protein From Fish Induces Cancer-like Skin Lesions in Mice
- Osteoarthritis and Effects of Estrogen Replacement Therapy on Cartilage
- Adolescent Suicide: Identifying Risks and Protectors
- Basic Fibroblast Growth Factor Stimulates Continued Growth of New Nerve Cells
- Brain Plasticity and the Very Early Perception of Speech
- Bullying Among Middle and High School Youth
- First National Data to Understand Where Children Drown
- New Clues Regarding the Role of Bacteria Infections in Premature Births
- Old Drug Offers New Hope to Victims of Childhood Neuro-Degenerative Disease
- New Evidence Shows Risk for Adult Hypertension and Cardiovascular Disease Begins Before Birth
- Activin Receptors – A New Anticancer Signal in Human Tumors
- Silencing of Apoptosis Genes in Childhood Brain Tumors
- Cell Phone Use Doesn't Increase Risk of Brain Tumors
- Identifying Gliomas That Will Respond to Chemotherapy
- How Cells Sense Oxygen
- Silicone Breast Implants Not Linked to Most Cancers or Increased Mortality
- Newly Discovered Gene for Juvenile Polyposis May Lead to Better Cancer Prevention and Clues about What Triggers Other Gastrointestinal Cancers
- Molecular Profiles Identify Genetically Distinct Subsets of Cancerous Tumors
- Medullary Pancreatic Cancer: A New Classification for an Old Disease
- New Findings on *BRCA2* Mutations and Hereditary Ovarian Cancer
- Racial and Ethnic Differences in Advanced-Stage Prostate Cancer
- Genetic and Structural Studies of Apert Syndrome
- Human Brain's Natural Painkiller System in Action
- Interaction Between Genes having Tumor Suppressor and Oncogenic Functions
- Mouse Model Sheds Light on Hereditary Dental Defect
- Natural Genetic Transformation of Oral Bacteria
- Scientists Sequence Genome of Major Periodontal Disease Bacterium
- Bringing Sleep into Focus
- Where does Visual Plasticity Occur in the Brain?
- The Timing of Visual Responses to Light
- Early Eye Development
- Discovery of Gene for Hallervorden-Spatz Syndrome
- Protection of the Lens by αA-Crystallin
- Myocilin in Aqueous Humor
- Growth Factors Prevent Alcohol's Brain Damage in Living Mammal Fetus
- An Appetite for Alcohol
- Craving for Alcohol Activates Specific Brain Areas in Alcoholics
- Alcoholics Have Changes in Activity of Brain's "White-Matter" Genes
- Closing in on Genes for Alcoholism
- New Non-invasive Method to Diagnose Pneumocystis carinii in Patients with HIV and Other Immunosuppressive Disorders
- Resistance Testing to Optimize Antiretroviral Therapy in HIV-Infected Patients Who Have Failed Prior Therapy
- Nitric Oxide Treatment Replenishes Blocked Nitric Oxide Synthesis and Maintains Vascular Blood Flow

- Mosquito Larva, Anopheles arabiensis, Growth in the Presence of Maize Fields
- The Neural Basis for Obesity and Other Weight Disorders
- Accuracy and Bias in Ratings of Nursing Home Residents' Pain
- Longitudinal Follow-up of Neonatal Intensive Care Unit Survivors
- Predicting Left Ventricular Hypertrophy in Young Hypertensive African-American Men
- Mouse Models of Insulin Resistance
- Integration of Diverse Signals Regulating Appetite and Body Size by the Brain
- Increasing Severity of Diabetes in Younger Native Americans
- Improved Long-Term Survival for Patients with Type 1 Diabetes
- Cholesterol Transport in Niemann-Pick Type C Disease
- Beta Cells that are Resistant to Immune-mediated Destruction
- Molecular Mechanisms of Cellular Copper Metabolism
- Effect of the Protease Inhibitor Indinavir on Import of Glucose into Muscle
- *Helicobacter pylori* Strains Influence Host Inflammatory Responses
- What Causes Polycystic Kidney Disease?
- Advances in Understanding the Function, Structure, and Genetics of the Urinary Bladder
- Genetic Link Discovered for IgA Nephropathy
- HIV-associated Kidney Disease and the Kidney as a Reservoir of Persistent HIV Infection
- Surprisingly Broad Potential Fates for Adult Stem Cells
- Hematopoietic Differentiation of Rhesus Monkey Embryonic Stem Cells in Culture
- Repairing Damage from Heart Attacks: Using Adult Bone Marrow Stem Cells in Mice
- Mouse and Rat Genome Sequences: Tools for Understanding the Human Genome
- Technique Can Distinguish Hereditary from Non-Hereditary Tumors: May Lead To New Diagnostic Tests for Breast Cancer
- Advances in Prostate Cancer Research
- Human Genome Project Develops Multimedia Educational Kit for High School Students and Public
- Gene Chips Accurately Diagnose Four Complex Childhood Cancers
- A Mouse Model Provides Insights about the Inner-ear Defects in Pendred Syndrome, a Genetic Disorder Associated with Deafness and Goiter
- Scientists Find a New Tumor Suppressor Gene Involved in Breast, Prostate and Other Cancers

Science Capsules

- Gene Therapy May Prevent Damage From Stroke
- Identifiable Illnesses from Hepatitis C Virus (HCV) Infection Take Many Years to Develop
- Where We Live Affects Our Cardiovascular Health
- "Early to Bed, Early to Rise" Gene Discovered
- Researchers Uncover a Secret of Burning Fat
- Understanding Bacterial Interactions has Potential to Help Cystic Fibrosis Patients
- Sensitivity to Salt Increases Risk of Early Death
- Tiny Air Pollutants Linked to Heart Attacks
- Inhaled Gas Displays Potential for Keeping Blood Vessels Open
- Gene Therapy Against Free Radicals May Prevent Vascular Damage
- Factors Influencing Lung Development and Injury Identified
- The Impact of Family Help on the Timing of Placement of Cognitively Impaired Elders in an Institution
- Decline in Severe Cognitive Impairment Among Older Americans
- Comorbidity and Breast Cancer in Older Women

- Aortic Stiffness and Visceral Adiposity in Older Adults Enrolled in Health ABC
- Cardiovascular Disease, Interleukin-6, and Risk of Mortality in Older Women
- Newly Understood Action of Sex Hormones Points the Way to New Treatment for Osteoporosis
- Importance of Local Estrogen Biosynthesis in Improved Cardiovascular Function
- Caloric Restriction Has No Adverse Effects on Skeletal and Reproductive Health in Rhesus Monkeys
- Familial Patterns and Protective Factors in Exceptional Longevity
- Chromosome 10 Contains New Risk Factor Genes for Late Onset Alzheimer's Disease
- RANTES Potentiates Antigen-Specific Peripheral and Mucosal Immune Responses
- Old and Young Humans Produce Similar Types of Antibodies
- Protein Switching Between Inactive and Active States
- Largest Membrane Protein Domain (19kDa) Determined by Solution NMR
- Key Mechanics of Cell Membrane Fusion Revealed
- On the Way to Making a Pancreas
- Drosophila Study Implicates New Genes in Human Neurodegenerative Disorders
- Sleepy Genes
- Controlling Zinc in Cells
- Discovery of a Key Step in Auxin Biosynthesis through Comparative Biochemistry
- Characterization of the Control of Telomeres in Drosophila
- Insight into How Clots are Dissolved
- Effect of Normal and Mutant MARCKS Protein on Cell Adhesion: Evidence for a Role in Brain Development
- Discovery of a New Cytochrome P450 Arachidonic Acid Hydroxylase in Brain
- Imaging Blood-Brain Barrier Function
- Regulation of Chondrocyte Development
- Decorin in Lyme Arthritis
- Green Tea and Cancer Prevention
- Molecular Genetic Basis of Sporadic Basal Cell Skin Cancer
- New Biologic Markers Characterized for Scleroderma
- A New Pathway to Increased Bone Density in Mice
- Difficulty Extracting Social Information from Faces Characterizes Autism
- Suppressing Unwanted Memories by Executive Control
- ADHD in Girls
- Making Employers Care about Mental Disorder Related Disability: The Problem of "Presenteeism"
- Molecules Mediating Synaptic Maturation Identified
- Cortical Plasticity Following Visual Experience
- Turning Perception into Action
- Overcoming Barriers to Access of Antiviral Therapy in Racial and Ethnic Minorities Infected with HIV
- Visual Discrimination Learning Requires Sleep After Training
- Recognition Memory
- How the Brain Encodes Abstract Rules
- A Role for Endogenous Cannabinoids in the Brain
- Transgenic Rat Model of the AIDS Virus
- Familial Dysautonomia Gene Discovery
- Flies and Brain Disorders
- Glia Regulate Synapses
- Glial Cells may be Culprits in Neuropathic Pain
- Visualizing Migraine Auras
- Pain Perception
- New Insights into Neurotransmitter Release
- Sleep and Brain Plasticity
- New Model System for the Study of West Nile Virus Encephalitis
- Gene Abnormality for Cystic Fibrosis May Be Responsible for Development of Chronic Sinusitis
- Inherited Mutation Linked to Increased Incidence of Lymphoma
- Exposure to High Levels of Cat Allergen Results in Protective Immune Response
- Identification of an Induced Cell Surface Channel on Red Blood Cells Infected with Malaria Parasites
- HIV Can Bind Efficiently to Immune Cells that Lack CD4, the Primary HIV Receptor

Molecule
- Determination of Differences in Cytotoxic T-Lymphocyte Responses in Early and Chronic HIV Infection
- Viral Fusion: New Clues on Influenza Entry into Cells
- Regulatory Pathway Identified that Controls Resistance to the Beta-Lactamase Class of Drugs in Staphylococcus aureus
- Controlling Inflammation by a Synthetic Molecule that Targets the Heart of the Process
- A Molecule Discovered on Immune Cells Plays a Central Role in Generating Antibodies
- Intravenous Immunoglobulin Prevents Inflammation through an Inhibitory Receptor Molecule
- Initiation of Smoking: Genes Play An Important Role
- Potential New Target for the Treatment of HIV
- Prenatal Exposure to Methamphetamine Increases Neurotoxic Risk for Male Offspring
- Morphine Can Alter Immune System Function: The Role of Substance P
- Hepatitis C Risk Is Not Limited to Those Who Inject
- Researchers Develop Antibodies that Recognize Hepatitis C Virus
- Experimental Animal Model Reveals Ability of Soy to Reduce Pain
- Mutated Gene Causes Sleep Disturbance
- Treatment for Persistent Asthma
- Orange Juice Alters the Metabolism of Certain Drugs
- Improving Understanding of Placenta Development
- Body Position Alters Heart Rate
- A Role for "Junk DNA:" Functional Significance of Repetitive DNA Elements in Eukaryotic Genomes
- Genomic Analysis of Radiation-resistant Bacterium: A Model Organism for Understanding Mechanisms of DNA Damage and Repair
- Bioinformatics Tools Provide Insight into the Mechanisms of Genome Evolution and Bacterial Pathogenesis
- Multilateral Initiative on Malaria
- Understanding Aromatase in Breast Cancer
- Markers for the Blood Vessels of Human Cancers
- A Functional Atlas for Caenorhabditis elegans
- Clues to Cancer Recurrence
- Chromosomal Instability in Cancer
- Protein Indicates Double-stranded DNA Breaks
- Prostate Cancer in African American Men
- Identification of a Novel Enzyme Active in Breast Cancer
- Steroid/Nuclear Receptors Function by Hit-and-Run
- Source of Gene Mutations Linked to Cancer
- Autoantigens in Sjögren's Syndrome
- Effect of Interleukin -1 in Periodontitis
- Gene Inhibits Invasion and Metastasis of Cancers
- New X-linked Recessive Immunodeficiency Defined
- Potential Role of Bone Proteins in Cancer
- Bacterial Interactions within Dental Plaque
- Self-Assembly Properties of Recombinant Engineered Amelogenin Proteins
- The Structure of Cell Membrane Water Channels
- Suppression of Specific Molecular Targets Improves the Success Rate of Corneal Transplants
- Genetic Ocular Disease of Native Americans
- Lens Cell Survival
- A World of Color
- Sight and Consciousness
- New Target for Therapy in Age-related Macular Degeneration
- Phagocytosis Pathway Dysfunction in Human Retinal Disease
- Hearing and Looking
- How do We Know that We've Seen?
- Speed of Light Responses
- A New Ethical Framework for the Conduct of Placebo Controlled Trials
- White Blood Cell Types that Have a Hand in Fighting Infections
- HIV Infection Increases the Risk of Transmission of Herpes and Cytomegalovirus (CMV) to Sexual Partners and Newborns
- Clinical Manifestations of HIV Infection in Thailand
- Understanding HIV-Related High-Risk

Sexual Behaviors Among Women in Bogota, Columbia
- HIV Protease Inhibitors Impair Fat Cell Development
- In-Utero Exposure to Diabetes Increases Offspring's Risk of Diabetes and Obesity
- Genetic Influence in Obesity and the Metabolic Syndrome
- Clinical Expression of Hereditary Pancreatitis
- Risk Factors for Primary Biliary Cirrhosis
- Brain Activity in Patients with Irritable Bowel Syndrome
- Gene Linked to Kidney Disease Caused by Diabetes
- Decade of ELSI Research Conference
- African-American Hereditary Prostate Cancer Study Network
- African-America Diabetes Mellitus Study (AADM)
- A Mouse Model for a Cancer Syndrome that Results in Multiple Endocrine Tumors
- Usher Syndrome Type 1D
- Functional Connectivity Between Brain Areas During the Visual Processing of Word and Word-Like Stimuli

Stories of Discovery

- How Sweet It Is!
- The Declining Disability of Older Americans
- The Human Genome, Chapter Two
- Environmental Agent Gives Clues to Arthritis, Depression, and Cancer
- How Ovaries Fail
- Determining the Genetic Cause of Drug-Resistant Malaria
- Accessing the Human Genome: Public Information Resources as Discovery Tools
- Providing Sight to Dog Born Blind
- Free Radicals: A Link Between Alcohol and Liver Damage
- Understanding Disease-Environment Interactions in Global Amphibian Decline
- A Fifteen Year Investment in Caregiving Research
- Bacterial Pili – Molecular Initiators of Bladder and Kidney Infections
- Genetic Breakthroughs in the Study of Crohn's Disease

Goal b) Develop new or improved instruments and technologies for use in research and medicine.

Science Advances

- Cancer-like Mutations Found in Patients with Sporadic Primary Pulmonary Hypertension
- New Technique for Characterizing Carbohydrates May Lead to New Pharmaceuticals
- Researchers Establish Requirements of Successful Gene Therapy for Beta-Thalassemia
- Umbilical-Cord Blood Can Be Used for Stem Cell Transplantation in Adults
- Laboratory Method Predicts Success of Umbilical Cord Blood Stem Cell Transplants
- Leukoreduction Does Not Benefit HIV-Infected Patients Requiring Blood Transfusions
- Hearing Aid Clinical Trial
- Abilities in Auditory Pitch Recognition are Largely Inherited
- Characterization and Functional Classification of 15,000 Mouse Genes
- The TAPP Mouse: The First Link between Plaque and Tangle Formation
- Pesticide Creates a Rat Model of Parkinson's Disease
- Detecting Lead Using DNA
- Model for Benzene Induction of Leukemia and/or Lymphoma
- Functional Analysis of Mutations in the p53 Tumor Suppressor Gene
- New Technique Could Enhance Practical Applications of Genetics
- Database Developed for Handling and Providing Initial Analyses of Microarray Data
- Developing Tools for Toxicogenomics: a DNA database for *Xenopus laevis*
- New Insight into Diseases of Aging Possible with Fluorescent Nanosensors
- Tissue Engineered Repairs of Articular Cartilage
- Chronic Wounds: Epidemiology and Treatment
- Progress Toward Gene Therapy of Genetic Diseases of Bone
- A Natural Resistance to Memory
- New Technique Identifies Gene Abnormalities in Schizophrenia
- Enhancing Reasoning with Transcranial Magnetic Stimulation (TMS)
- Stem Cells Show Promise for Treating Diabetes
- Pesticides and Parkinson's Disease
- Gene Microarray Analysis of Brain Tumors
- Understanding Functional Magnetic Resonance Imaging (fMRI) of the Brain
- Brain Images of Children Prenatally Exposed to Methamphetamine Reveals Alteration in Brain Chemicals
- New Technology May Help Increase the Accuracy of Determining Prenatal Drug Exposure
- Automated Synthesis of Complex Sugars
- Mechanism of Protein Degradation in the Proteasome
- New Approaches to Integrated Protein Separations and Mass Spectrometry
- Electron Microscopy Used to Model the Fine Structure of Insulin-secreting Cells
- New Imaging Technique Allows Researchers to Follow Stroke in Progress
- Computer Technique Helps Researchers Diagnose Cervical Ectopy
- Methods for Unraveling Protein Structure and Function
- New Developments in the Evolutionary Classification of Proteins from Complete Genomes
- A Powerful Tool for Identifying Sequence Similarities
- New Modeling Tools for Analyzing Tumor DNA Data
- ClinicalTrials.gov
- Profiles in Science
- Clinical Proteomics Initiative
- Controlled Growth Factor Release System
- Mouse Epidermal Stem Cell Sorting
- Mussel Byssal Thread: A Self-Healing Biomolecular Material

- New Evidence of the Existence of Circulating Skeletal Stem Cells
- Potential Gene Therapy for Dominantly-Inherited Retinal Diseases
- Improved Imaging of the Human Lens
- Gene Regulation in the Retina
- Inhibition of Neovascularization in the Eye
- Decreased Haze and Apoptosis After Photoablation
- Inhibition of CMV Replication
- New Focus on Race Yields Better Data on Cirrhosis
- A Computer "Detective" Helps Physicians Locate Colonic Polyps at Virtual Colonoscopy
- HIV Infection Among Blood Plasma Donors in Rural China
- The Effects of Chernobyl Radiation on Thyroid Cancer
- A Model to Predict Survival in Patients with End-Stage Liver Disease

Science Capsules

- Animal Models Show Role of Estrogen in Body Fat Accumulation with Age
- A Fly Model of Tau Neurodegeneration
- New Insights Into How a Gene Protects Our Health
- Cloning Mouse Genes to Study Skin Cancer
- Low Growth-Hormone Response to Pharmacological Challenge May be a Reliable Biological Marker in Childhood Depression
- Novel PET Ligands to Image the D4 Dopamine Receptor in Brain
- MRI Analysis Tools To Aid Developmental Neuropsychiatric Studies
- Getting to the Right Place: A Novel Method to Sort Out Protein Localization
- Culturing Progenitor Cells from the Human Brain after Death
- Turning Blood into Brain
- Highly Sensitive Solid State NMR
- Next Generation Internet Implementation to Serve Visible Human Dataset
- Remote Radiation Treatment Planning System
- Mammography for the Next Generation Internet
- Tribal Connections
- Internet and Web Performance Evaluation
- Rapid Identification and Characterization of Genetic Variations
- New Database for Identification of Prostate Cancer Biomarkers
- Development of Silk-Based Biomaterials for Bone Formation
- Infrared Lasers Used for the Removal of Carious Hard Tissue
- New Cell Culture Process Offers Promise for Immunotherapy of Cancer
- A Stimulating Way to Donate Blood
- A New Approach for Selecting Best Treatment Regimen When Using Therapeutic DNA Damaging Agents
- Developing Electronic Patient Records Systems for Public Health Survillance and Clinical Care
- Non-invasive Technique to Detect Hypoglycemia in Patients with Diabetes
- New Clinical Laboratory Test for Measuring Serum Cholesterol in Lipoprotein Fractions

Stories of Discovery

- Glimpses into the Working Brain: The Development of Neuroimaging Tools to Advance Our Understanding of Addiction
- MEDLINE and MEDLINEplus: A Continuing Story of Discovery
- Hearing Aids – How Basic Biology Translates into Technology to Help the Hearing Impaired

Goal c) Develop new or improved approaches for preventing or delaying the onset or progression of disease and disability.

Science Advances

- Enzyme Essential for Muscle Nourishment is Inactive in Children with Duchenne Muscular Dystrophy
- Reduced Fat Intake to Lower Cholesterol is Safe and Beneficial for Children
- When it Comes to Exercise, Every Little Bit Helps To Prevent Coronary Heart Disease
- Counseling Helps Women, But Not Men, Improve Fitness
- Mediator of Transfusion-Induced Fever is Identified
- Symptomatic Congenital Cytomegalovirus Infection in Infants of Women with Preconceptional Immunity
- Effects of Socioeconomic Status on Aphasia Severity and Recovery
- Spoken and Written Language Disabilities in School-Aged Children
- Phase I Clinical Trial of an Otitis Media Vaccine Candidate
- Physical Exercise Prevents Disability in Older Persons with Arthritis
- Reducing Delirium after Hip Fracture in Older Adults
- Psychological Benefits of Exercise in the Elderly
- Women Caring for Family Members with Dementia Can Benefit from an Exercise Program
- Estrogen May Attenuate the Age-Associated Systolic Blood Pressure Rise in Post-Menopausal Women
- Dietary Restriction Increases Levels of Growth Factors in the Brain and Stimulates Production of New Nerve Cells
- Vaccination with Amyloid-beta Peptides Prevents Age-related Memory Deficits in a Transgenic Animal Model of Alzheimer's Disease
- Environment May Protect Against Cognitive Decline and Alzheimer's Disease (AD)
- Statins May Reduce the Risk of Alzheimer's Disease
- Small Particles in Air May Trigger Heart Attacks
- Women's Cancer Risk Linked with Nitrate Levels in Drinking Water
- The DDT Metabolite Associated with Increased Risk of Premature Birth
- Modest Increases in Ambient Ozone Concentration are Associated with Increases in School Absenteeism
- Variations in the Gene for Microsomal Epoxide Hydrolase:Possible Answer to "Why Me?"
- Amphibian Deaths Linked to Global Climate Change
- In utero and Postnatal Exposure to Polybrominated Biphenyls Causes Early Puberty in Girls
- Risk Factors for Asthma Identified
- Are Plasticizers in the Environment Making You Infertile?
- Genistein, a Plant Estrogen Found in Soy Products, Increases Cancer in Animals
- Two Dietary Plant Estrogens Increase Cancer Risk in Mice
- Simple Steps Can Reduce Dust Mite Allergen Exposure in Low Income, Urban Homes
- The Effects of Implant Wear Particles on Bone Cells
- Molecular and Psychological Influence on Barrier Function of Skin
- Osteoarthritis in Young and Middle-aged Women
- Effect of Dietary Protein on Bone Loss in Elderly Men and Women: The Framingham Osteoporosis Study
- Jumping Improves Hip and Spine Bone Mass in Prepubescent Children: A Randomized Controlled Trial
- How are Mental Disorders and Violence Related?
- Preventing Chronic Depression and Substance Abuse
- Negative Impact of Parental HIV Illness Can Be Prevented in Their Children

- Protecting the Brains of Infants During Surgery for High-risk Heart Defects
- Another (Running) Step Towards Protecting the Brain in Ataxia-Telangiectasia
- Dietary Supplement for Brain Injury and Disease
- The Brain's Dopamine Neurons Require Estrogen
- Managing Chronic Tension-type Headache
- Transient Ischemic Attacks Warn of a High Risk for Stroke
- A Vaccine is Highly Effective for Preventing Ebola Virus Infection in Primates
- A Live Attenuated Dengue Virus Vaccine Candidate is Safe and Stimulates a Protective Immune Response in Human Volunteers
- Use of Umbilical Cord Blood as a Source of Stem Cells for Transplantation
- Public Service Announcements Geared to Address Teens' Specific Motivation to Use Drugs Can Reduce Drug Use
- Advances in Development of an AIDS Vaccine
- Steroid-free Immunosuppression for Kidney Transplantation in Children
- Less Estrogen for Osteoporosis
- Maternal Antibody Can Protect Newborns Against Diseases Like Meningitis, Pneumonia, and Blood Stream Infections
- HIV Prevention Program Helps Reduce Sexual Activity Among Minority Youth
- Virginity Pledges Help Some Adolescents Delay Sexual Activity
- Early Childhood Program Reduces Crime and Dropout Rates
- A Potential DNA Vaccine for AIDS
- Study Documents Strong Association Between Cigarette Promotion and Initiation of Smoking in Adolescents
- Rebelliousness and Risk-taking in Fifth Graders Predict Cigarette Smoking by Twelfth Grade
- Relatives of People with Pancreatic Cancer are Probably at Increased Risk of the Cancer
- Obesity and Hypertension Increase Risk of Kidney Cancer Among Men
- Association of Cancer with AIDS-Related Immunosuppression in Adults
- Smokeless Tobacco Use as a Gateway for Smoking Initiation
- Association between Human Papillomavirus and a Subset of Head and Neck Cancers
- A Protein Associated with Atherosclerosis May Give New Insights into Glaucoma
- Spread of Ocular Herpes Simplex Virus Infection in Mice and Humans
- Proyecto Vision Evaluation and Research
- Violent Assaults and Car Crashes Drop in Communities that Have Comprehensive Alcohol-Prevention Program
- Policy Changes Reduce Underage Drinking
- Early-Onset Drinkers Take More Risks, Sustain More Injuries
- HIV Transmission in Russia
- Drug Use and the HIV Epidemic in Northern Vietnam
- Effective Means of Responding to Resurgence of Dengue
- Effective Means of Responding to Resurgence of Dengue
- Improving Mobility of Nursing Home Residents with Alzheimer's Disease
- Psychologic Change in Children with Acute Lymphoblastic Leukemia
- Psychosocial Nursing Therapy after Cardiac Arrest: Impact on Two-Year Survival
- Targeting Adolescents in Order to Achieve Diabetes Treatment Goals
- Outcomes of Advanced Practice Nurses in Long-term Care Facilities
- Postpartum Smoking Behaviors and Immune Response in Mothers of Term and Preterm Infants
- Reducing the Risk of Heart Disease in Women with Type 2 Diabetes
- Breast Feeding May Limit Teenage Obesity
- ACE Inhibitor Reduces the Risk of Kidney Failure in African Americans with Hypertension
- A New Way to Prevent Blood Transfusion Reactions

Science Capsules

- Eating Fish Reduces Risk of Stroke
- DASH Hypertension Diet Also Lowers Cholesterol
- Reducing Sodium Leads to Substantial Drop in Blood Pressure
- Weight Loss Reduces Risk of Sleep Apnea
- Raloxifene Does Not Affect Cognitive Function in Postmenopausal Women
- Positive Emotions in Early Life Linked to Longevity
- Depression and Agitation in Alzheimer's Disease: Effects on Caregivers
- Alzheimer's Disease Transgenic Model Immunization: Non-Toxic Peptide Vaccine
- Molecular Basis of Alpha Virus Assembly
- Quicker Cancer Assays Possible with Genetically Altered Mice
- Important Insight into Food Poisoning
- Environmental Agent Inhibits Testosterone Production
- Risky Health Practices in Adult Men Traced to Their Experiences as Children
- How Does Depression Contribute to Mortality in Older Adults?
- Perceived Stigma Can Affect Treatment Adherence for Depressed Older Adults
- Keys to Successful Aging: Results of a 60-Year Prospective Study
- Isolation of a Potential Vaccine Candidate Against *Leishmania*
- Improved TB Vaccine Provides Enhanced Protection
- Families Can Provide a Shield Against A Child's Initial Drug Use
- Drug Users in Communities with Low HIV Rates More Likely to Engage in High-risk Behaviors
- Being Overweight at Age 13 Predicts Insulin Resistance at Age 22
- Dental Plaque Formation: Pellicle Protein Characterization
- Increased Risk for Bone and Liver Cancers in Nuclear Plant Workers
- Cancer Risk in DES-exposed Mothers
- Hereditary Retinoblastoma and Lung Cancer Risk
- Genetics and Nicotine Addiction
- New Cytotoxins for Tumor Cells
- Long-term Estrogen Replacement Therapy Reduces the Risk of Cataracts
- Vaginal Delivery After a Cesarean Section
- Depression Intervention in College-age Women
- Exercise Can Safely Help HIV+Patients Maintain Weight and Endurance
- Managing Cardiovascular Risk Factors During Encounters for Coronary Bypass Surgery
- Reducing Incontinence Among People at Home With Dementia
- Advance Directives Help Lower Stress Levels in End-of-Life Decisions
- Reducing Cardiovascular Risk in Overweight Older Women
- Effect of School-Based Programs on Suicide Prevention
- Trends of Cigarette Use in Adolescents
- Employment has Little Effect of High-Risk Pregnancy Outcomes
- Drug Ototoxicity

Stories of Discovery

- Preventing Strokes
- The Ominous Link between Obesity and Type 2 Diabetes
- The Maternal Side of Mother to Child HIV Transmission
- Understanding What Goes Wrong in PTSD: Pathways to Prevention
- Parkinson's Disease – Identifying the Environmental Triggers Genetic and Molecular Basis of Longevity

Goal d) Develop new or improved methods for diagnosing disease and disability.

Science Advances

- Blood Test Can Predict Pulmonary Complications from Sickle Cell Disease
- Newly Identified Genetic Defects Cause Sudden Cardiac Death in Young People
- Genetic Mutation Increases Heart Attack Risk for Women on Hormone Replacement Therapy
- MRI Helps Identify Patients Likely to Benefit from Revascularization
- Preschool Communication Problems and Later Academic Performance
- Development of Stereocilia Orientation in Hair Cells
- Loss of Neurons in a Particular Brain Region is Associated with Onset of Cognitive Decline in Older Individuals
- Some People with Mild Cognitive Impairment Progress to Alzheimer's Disease and Some Don't: How to Tell
- Imaging Clearance of Plaques by Immunotherapy in Living Mice
- Imaging Small Regions of Brain in Humans and Genetically Modified Mice
- Bacterial Slime Clogs Cystic Fibrosis Lungs
- Identification of a Genetic Risk Factor for Lumbar Disc Disease
- Genetic and Molecular Basis of Pseudoxanthoma Elasticum
- Epidermolysis Bullosa: Molecular Mechanisms and Treatment Possibilities
- Low Serum Thyroid Stimulating Hormone Levels Increase Risk of Fracture in Elderly Women
- Racial Disparities in the Diagnosis and Treatment of Schizophrenia and Depression
- Bipolar Disorder in Children: Exploring a New Diagnostic Entity
- Improved Diagnosis of Oligodendroglioma
- Predicting Intractability of Epilepsy in Children
- Link Between a Common Sleep Disorder and a Risk Factor for Alzheimer's Disease
- Early Prediction of Stroke Recovery
- Predicting Prognosis in Wilm's Tumor
- A Noninvasive Test to Detect Kidney Transplant Rejection
- Marijuana Use in Early Adolescence Can Lead to Pscychiatric Problems as an Adult
- Brain Damage Due to Methamphetamine Abuse Has Functional Consequences
- Understanding E. Coli Pathogenicity
- Diagnosing and Monitoring Sleep Apnea
- A New Device for Cancer Diagnosis
- Type 2 Diabetes Detection in High-Risk Individuals
- Improved Prediction of Tissue Damage in Stroke Patients
- Childhood Origins of Health Disparities in African Americans
- New Method to Measure Testosterone Levels May Help Diagnose Infertility in Men
- Artificial Intelligence in the Diagnosis of Breast Cancer
- HPV Testing Identifies Pap Test Abnormalities Needing Follow-Up
- New, Highly Accurate Technique for Genetic Diagnosis of Cancer Risk
- MR Imaging in Metastatic Lymph Node Detection and Gene Therapy
- Potential Biomarkers to Detect Early Ovarian Cancer Found
- Genetic Testing of Stool Detects Colorectal Cancer
- Use of Saliva in Diagnosis and Management of AIDS
- Early Detection of Head and Neck Squamous Cell Carcinoma
- Ultrahigh Resolution Instrument May Improve Diagnosis of Retinal Diseases
- Simpler Method of Genotyping Hepatitis C (HCV)
- Penicillin Resistant Meningitis in Salvador, Brazil
- Accuracy and Bias in Ratings of Nursing Home Residents' Pain
- Longitudinal Follow-up of Neonatal Intensive Care Unit Survivors

- Predicting Left Ventricular Hypertrophy in Young Hypertensive African-American Men

Science Capsules

- A Large-Scale Analysis of Gene Expression in Ovarian Cancer Suggests Novel Pathways and Reveals Novel Markers for this Disease
- Racial Differences in Cognitive Performance in Elders Disappear when Quality of Education is Assessed
- MAD2 Gene Linked to Genomic Instability in Aggressive, Drug Resistant Tumors
- Familial Mania Predicts Switch from Childhood Depression to Adolescent Bipolar Disorder
- Schizophrenia May Not Cause Long-term Cognitive Decline
- Gene for Myotonic Dystrophy Type 2
- Imaging Stroke Recovery
- Some Adolescent Smokers May Be Self-medicating
- Measuring Progression of Alzheimer's Disease
- Screening for Hemochromatosis
- Characterization of the Autism Gene
- Ductal Lavage for Breast Cancer Diagnosis
- A Possible Marker for Invasive Breast Cancer
- Invasion-specific Markers for Pancreatic Cancer
- Device May Enable Detection of Lung Cancer From Chest X-Rays
- Detection of Cancer-Predisposing Mutations in Mitochondrial DNA
- Development of Simple and Reliable HIV Test for Resource Poor Settings
- Prenatal Stress and Outlook Affects Birth Outcomes in High-Risk Pregnancies
- Genetic Analysis of Digestive Physiology Using Fluorescent Lipids
- Bladder Cancer Diagnosed by Simple Urine Test
- A New Way to Monitor Progression of Polycystic Kidney Disease

Stories of Discovery

- Single Nucleotide Polymorphisms (SNPs) and Haplotypes: New Tools for Tracing Inherited Diseases
- Mass Spectrometers Weigh the Evidence for Health and Disease

Goal e) Develop new or improved approaches for treating disease and disability.

Science Advances

- Revascularization Saves Lives of Heart Attack Patients Experiencing Cardiogenic Shock
- Gene Therapy May Save Diabetic Patients' Legs
- Beta-Blocker Does Not Increase Survival of Black Patients with Advanced Heart Failure
- Inhaled Corticosteroids are Safe and Effective for Children with Asthma
- Inhaled Corticosteroids Do Not Slow Progression of COPD
- Arginine Supplements May Benefit Patients with Sickle Cell Disease
- New, Low Cost Immunosuppressive Therapy for Aplastic Anemia is Deemed to be "Dangerous"
- Gene Therapy and Aminoglycoside Protection
- Complete Remission and Preservation of Voice and Speech in Patients with Head and Neck Cancer Using Chemotherapy and Radiation
- Clinical Trial Underway for a New Drug for Treatment of Patients with Vocal Tract (Head And Neck) Cancer
- Prevalence of Otitis Media in Childhood and Treatment
- Working to Cure Prion Diseases
- Low-dose Estrogen Reduces Bone Breakdown in Older Women
- Potential New Treatment for Type 2 Diabetes Mellitus in the Elderly
- Copper/Zinc Chelator Reduces Amyloid Accumulation in Transgenic Mice
- Melatonin Helps Some Older Insomniacs Sleep Better
- Old Drugs Learn New Tricks
- Tiny Nanotubes as New Antibiotics
- New Insights Into Why Medicines Work Differently Among People
- Reversal of Diet-induced Insulin Resistance: Another Use for Aspirin?
- Forced Limb-use Studies in Rats May Have Implications for Parkinson's Disease
- Controlling Taxol's Toxicity in Breast Cancer Treatment
- Combination Therapies for AIDS Patients – How Toxic are They?
- Drug Treatment of Lead-exposed Children Does Not Improve Psychological Test Scores
- Toxic Effects Caused by Drugs Used to Treat AIDS
- Reducing Side Effects of Drugs – Drug Metabolism Variations Identified
- Regulation of Cartilage Induction
- Insights into the Pathogenesis of Marfan Syndrome, a Heritable Disorder of Connective Tissue
- Gender, Catastrophizing, and Pain in Osteoarthritis
- Early Mortality in Systemic Lupus Erythematosus in Three Ethnic Groups
- Activated Immune Cells in Pathogenesis of Duchenne Muscular Dystrophy
- Skin and Muscle Coverage of Severe Leg Injuries
- Investigating the Treatment of Alopecia Areata in Mouse Model Systems
- Treatment for Psoriasis
- New Therapy for Lupus Tested in Mice
- Administration of Parathyroid Hormone Reverses Bone Loss in Osteoporotic Women
- Mechanism of Parathyroid Hormone to Increase Bone Mass Clarified
- Treating Insomnia with Cognitive Behavioral Therapy, Not Medications
- Parsing PACT: What Are the Critical Components of Holistic Community Care for SMI?
- St. John's Wort May Interfere with the Effectiveness of Prescription Medications
- Medication and Psychotherapy Effective in Treating Children and Adolescents With Anxiety Disorders
- Improving Chances for Employment: Negative Symptom/Positive Symptom Reductions in Schizophrenia

- Reducing Individual and Societal Burden of Depression: Results from a Community Primary Care Intervention Trial
- Improved Diagnosis of Ataxia May Identify a Treatable Subtype
- New Understanding of Inflammatory Pain
- Learning From "Negative" Clinical Trials
- Moving Towards Drugs for Prion Diseases
- Chronic Lyme Disease Symptoms Not Improved by Intensive Antibiotic Treatment
- New Compound Blocks Marijuana's High
- Reducing Women's Concern About Weight Gain Improves Smoking Cessation Rates
- Addiction Treatment Programs Specifically Tailored to Adolescents Can Be Effective in Reducing Drug Use, Criminal Activity, and Improving School Performance
- Treating African-Americans with Kidney Disease Due to High Blood Pressure
- Structural Insight into Improving Cholesterol-Reducing Medicines
- Coagulation Factor VIII Gene Transfer in Severe Hemophilia A
- Candidate Drug for Treatment of Lupus
- Recovery of Breathing Function in Spinal Cord Injured Patients
- Testosterone Protects Against the Cancer-Causing Effects of Estrogen on Breast Tissue
- New Treatment Increases Chances For Pregnancy in Women With Polycystic Ovary Syndrome
- Tubal Sterilization Does Not Increase the Risk of Menstrual Abnormalities
- Low-Cost Supplement is Effective in Improving Child Health in Developing Countries
- Androgen Blockers Can Help Women With Infertility Caused By Polycystic Ovary Syndrome
- Study Suggests Lumpectomy is at Least as Cost-Effective as Mastectomy When Long-Term Medical Care Costs Are Considered
- Immunotoxin Yields Promising Results Against Hairy Cell Leukemia in Early Trial
- Treatment to Boost Immune Actions of Blood-producing Cells May Improve Breast Cancer Therapy
- Vaccine Made from Pancreatic Tumor Cells of Several People May Stimulate Immune System to Attack Pancreatic Cancer
- Vaccines for Lung and Colon Cancer Show Promise
- Vaccines for Melanoma Patients
- Beehive Product May Inhibit Dental Caries
- Cellular Communication in Dental Plaque
- Fibrous Dysplasia of Bone
- Novel Mechanism of Tumor Suppression in Oral Cancer Cells
- Potential Use of Human Dental Pulp Stem Cells in Tissue Engineering
- Targeted Drug Delivery to Head and Neck Tumors
- Collaborative Ocular Melanoma Trial
- Protein Involved in Cell Migration in Wound Healing May Inhibit Tumor Growth
- Therapy for Retinal Degeneration
- Improving the Effectiveness of a Costly Treatment
- Supplement Given After Birth Prevents Neuro Defects in Mammalian FAS Model
- Widely Used Herbal Remedy, St. John's Wort, Does Not Interfere With Anti-Epileptic Drug
- Cooking Tumors with Needles: Minimally-invasive, Image Guided Tumor Ablation with Radiofrequency Current
- Long-Acting Antifolate Compared to Shorter-Acting Antifolate for Drug Resistance
- Predictors of Adherence and Plasma HIV Concentrations
- Dementia Family Caregiving Training: Caregiving and Caregiver Outcomes
- Specialized Home Care Intervention Improves Survival Among Older Post-Surgical Cancer Patients
- Relaxation and Music Reduces Postsurgical Pain
- Postoperative Pain Influences Tumor-Promoting Effects of Surgery
- Uncoupling Proteins: A New Way to Burn Fat?
- Alternatives to Pancreatic Islets: Stem Cells and Bioengineering
- Safe and Effective Therapy for Fabry Disease

- Benefits of Antiretroviral Therapy in HIV-positive Children
- Increased Risk of Cardiovascular Disease in HIV-Positive Patients with Fat Redistribution Associated with Antiretroviral Therapy
- Urinary Tract Infection: Recurrence, Anti-microbial Resistance, and Self-treatment
- Analysis Suggests That Previous Kidney Dialysis Shortens Survival of Subsequent Kidney Transplant Grafts

Science Capsules

- Sugar May Help Cystic Fibrosis Patients Avoid Infection
- Studies Reveal Differences in Effectiveness of Common Asthma Treatments
- Phenserine Regulates Translation of -Amyloid Precursor Protein Message: A New Target for Alzheimer's disease Drug Development
- Cytokine TGF- 1 Reduces Plaque Burden in Transgenic Mice
- Treating the Catabolic Effects of Burns
- Cognitive-Behavioral Therapy for Treatment of Bulimia Nervosa
- "Continuation Phase" Psychotherapy Can Help Prevent Recurrence of Depression
- Depression in Alzheimer's Disease Patients Is Treatable
- Antisense Therapy May Make Sense for Alzheimer's Disease
- Neurotrophins and the Blood-brain Barrier
- Encouraging Nerve Cells to Grow with Integrins
- Stretching Nerve Fibers to Help Them Grow
- Less Toxic Treatment for Patients with Chronic Granulomatous Disease
- Structured Intermittent Therapy Can Control Simian Immunodeficiency Virus in Monkeys
- Early Treatment of HIV-1 Leads to Augmented Immune Responses in the Chronic Phase of Infection
- Higher Dose of Acyclovir Proves Effective Against Newborn Herpes Virus Infections
- Successful Gene Therapy Prevents Kidney Rejection in a Large Animal Model
- Incentive to Work Helps to Keep Addicts Drug Free
- The Consequences of Stroke Reduced in an Animal Model System
- Nutritional Supplement Shows Promise as Treatment for Huntington's Disease
- Labeling of Dietary Supplements May Differ from Actual Contents
- Botanicals Used in the Treatment of Menopausal Symptoms Possess Estrogenic Activity
- Better Treatment for Blacks With Chronic Hepatitis C
- Prolonged Antibiotic Therapy Ineffective in Lyme Disease
- Chemotherapy and Cognitive Function
- Mechanism of HIV Drug Resistance
- Interleukin 15 May Play A Role in Some Leukemias
- Melanoma and the p53 Gene
- Nephrectomy and Advanced Renal Cell Cancer
- Role for p38 Kinase Signaling in the Cellar Responses to Cytotoxic Agents
- Improved Outcomes for Children with a Deadly Form of Leukemia
- Low-fat, High-fiber Diet Does Not Reduce the Risk of Precursor to Colorectal Cancer
- Combination Therapy Improves Outcomes for Patients with Stomach Cancer
- Yeast Vaccine Stimulates the Immune System Against Cancer Cells
- New Protein Promotes Corneal Wound Healing
- Antigene Radiotherapy for Multidrug-resistance in Cancer Through Use of New Radiopharma-ceuticals
- Workplace Issues Affect Nurse Workforce
- Transitional Care Model
- Folate Levels Related to Restless Legs Syndrome in Pregnant Women
- Comparing Costs of Birth Centers to Traditional Maternity Care

- Expansion of Umbilical Cord Stem Cells for Transplantation

Stories of Discovery

- Statins: They're not Just for High Cholesterol Anymore
- Enhancing Treatment Adherence in AIDS and Schizophrenia
- A Brighter Future for People with Lupus as a Result of Medical Research
- Bringing a New Medication to Market: Shifting Treatment From Clinics to Doctors' Offices
- NIH Scientists Develop the First Typhoid Vaccine that Protects Children Under Age Five
- Making Drugs Safe for Children
- The Story of Gleevec
- Salivary Glands: Potential Target Site for Gene Therapies

Appendix 7

Listings of Workshops and Other Meetings Convened by NIH Institutes and Centers

Research Goal A: ***Add to the Body of Knowledge About Normal and Abnormal Biological Functions and Behavior***	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
RFA, Exploratory Research on Fascioscapulohumeral Muscular Dystrophy – November 2000	Conference on the Cause and Treatment of Facioscapulohumeral Muscular Dystrophy – May 2000
RFA, Bone Formation and Calcification in Cardiovascular Disease – January 2001	NIH Institutes Working Group – September 1999
RFA,Neuropsychiatric Systemic Lupus Erythematosus – July 2001	Scientific Workshop on Neuropsychiatric Manifestations of Systemic Lupus Erythematosus – May 1999
PA, Midcareer Investigator Award in Patient-Oriented Research for Researchers in Female Pelvic Floor Disorders (K24) – April 2001	Pelvic Floor Disorders Workshop – September 1998
PA, The Zebrafish as an Animal Model for Development and Disease Research – May 2001	Functional Genomics Workshop – September 1999
PA, Exploratory/Developmental Award in Epilepsy Research for Junior Investigators – June 2001	Curing Epilepsy: Focus on the Future – March 2000
PA, Restless Leg Syndrome and Periodic Limb Movement Disorder – May 2001	Movement Disorders in Sleep: Restless Leg Syndrome – October 1999
RFA, Effects of Hypoglycemia on Neuronal and Glial Cell Function – July 2001	Hypoglycemia in the Brain – September 2000
RFA, International Bioethics Education and Career Development Award – August 2001	Global Forum for Bioethics in Research – October 2000
RFA, International Malaria Research Training Program – February 2001	•Workshop on Pathogenesis of Malaria Anemia – May 2000 •Malaria Anemia Session, 43rd Annual American Society of Hematology Meeting – December 2001
RFA, International Tobacco and Health Research and Capacity Building Program – June 2001	•Report on Cardiovascular Disease Prevention – 1998 •Working Group to Identify Research Fields and Public Health Data with the Highest Potential to Affect Tobacco Control Policy •Regional Workshops Convened by the Research for International Tobacco Control Group
Notice, Integrative and Collaborative Approaches to Research – October 2000	National Advisory General Medical Sciences Council Subcommittee Meetings – April 1998
RFA, Reannouncement of Large-Scale Collaborative Project Awards – February 2001	National Advisory General Medical Sciences Council Subcommittee Meetings – April 1998
RFA, Centers of Excellence in Complex Biomedical Systems Research – January 2001	New Approaches to the Study of Complex Biological Processes – February 1998
PA, Single Molecule Detection and Manipulation – February	Workshop on Single Molecule Detection and Manipulation

Research Goal A: Add to the Body of Knowledge About Normal and Abnormal Biological Functions and Behavior	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
2001	Workshop – April 2000
RFA, Exploratory Studies of Sustained Caloric Restriction in Non-Obese Persons: Physiologic Effects and Comparisons/Interactions with Physical Activity – October 2000	Caloric Restriction Clinical Implications Advisory Group – March 1999
PA, Biology of the Menopausal Process and Associated Health Conditions During and After Menopause – March 2001	International Conference on Biology of Menopause – September 1998
RFA, New Research Strategies in Osteogenesis Imperfecta – December 2000	Therapeutic Success in Treating Osteogenesis Imperfecta – September 1999
RFA, Studies of Sensory-Motor Functions Responsive to Gravity in Genetically Altered Model Systems – October 2000	Role of Transgenic and Knockout Studies in Understanding Sensory-Motor Performance in Altered Gravitational Performance – June 1999
PA, Physical Activity and Obesity Across Chronic Diseases – November 2000	Physical Activity and Obesity – 1992
RFA, Depression and Mental Disorders in Diabetes, Renal Disease, and Obesity/Eating Disorders – September 2001	Depression and Mental Disorders in Diabetes, Renal Disease, and Obesity/Eating Disorders – January 2001
RFA, Innovative Use of Non-mammalian Model Organisms to Study Membrane Transport – September 2000	Advances in Membrane Transport – December 1999
RFA, Cardiovascular, Lung, and Blood Immunobiology in Health and Disease – January 2001	•Workshop on Mechanisms of Proliferative and Obliterative Vascular Diseases – July 1997 •SPARK Working Group – September 1998 •Workshops on "Pulmonary Immunobiology and Inflammation" and "The Role of the Polymorphonuclear Leukocyte in Sickle Cell Disease" – July 1999
RFA, Susceptibility to Target Organ Damage in High Blood Pressure – January 2001	Workshop on Genetic Basis of Variability of Progression and Outcome in Heart, Lung, and Blood Diseases – July 1998
RFA, Mechanisms Underlying the Innervation of Specific Taste Receptor Cells – November 2000	Symposium at the Annual Meeting of the Association for Chemoreception Sciences – April 2000
RFA, Integrative Neuroscience Initiative on Alcoholism – January 2001	National Advisory Council Working Group on Research Priorities – March 2000
RFA, New Approaches to Developing Pharmacotherapy for Alcoholism – September 2001	National Advisory Council Working Group on Research Priorities – April 2001
Notice, Type I Diabetes Murine Model Resource: Notice of Limited Competition – July 2001	Type I Diabetes Mouse Model Resource Workshop – July 2001
Broad Program Announcements for Funding Opportunities Applicable to Brain Tumors and Pancreatic Cancer – Added to existing announcements in 2001	•Report from Brain Tumor Progress Review Group, "Report of the Brain Tumor Progress Review Group" – November 2000 •Report from Pancreatic Cancer Progress Review Group, "Pancreatic Cancer: An Agenda for Action" – February 2001
RFA, Exploratory/Development Grants in Social Neuroscience – September 2001	•Social Neuroscience – February 2000 •Social Cognitive Neuroscience – April 2001
PA, Behavioral, Social, Mental Health and Substance Abuse Research with Diverse – May 2001	New Approaches to Research on Sexual Orientation, Mental Health, and Substance Abuse – September 1999

Research Goal A: Add to the Body of Knowledge About Normal and Abnormal Biological Functions and Behavior	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
PA, Basic and Applied Research Related to ADHD – April 2001	Interdisciplinary Research on Attention-Deficit Hyperactivity Disorder – March 2000
RFA, Interdisciplinary Research Networks on ADHD – July 2001	Interdisciplinary Research on Attention-Deficit Hyperactivity Disorder – March 2000
RFA, Modular Phenotyping for Major Mental Disorders – September 2001	Treatment Development Workgroup Meetings – June and August 2001
RFA, Sex-Based Differences in the Immune Response – February 2001	•Gender and Autoimmunity Meeting – September 1995 •Task Force on Gender, Multiple Sclerosis and Autoimmunity – February 1999
RFA, Non-Human Primate Tolerance Cooperative Study Group – January 2001	Expert Panel on Immune Tolerance – February 1998
RFA, Infectious Etiology of Chronic Diseases: Novel Approaches to Pathogen Detection – February 2001	•Emerging Issues in Microbial Infections and Cardiovascular Diseases – October 1998 •New Approaches to Identifying Etiologies of Chronic Diseases – June 1999 •Crohn's Disease: Is There a Microbial Etiology? – December 1998
RFP, Leprosy Research Support & Maintenance (Armadillo Colony in the Post-Genome Era) – July 2001	Workshop on Leprosy Research in the Post-Genome Era – November 1999
RFA, Research on GHB (gamma-hydroxybutyrate) and its Precursors – January 2001	Cutting Edge Seminar: All about GHB – June 2000
RFA, Responding to Club Drugs and other Emerging and Current Drug Abuse Trends – January 2001	•Steroids Press Conference and Scientific Meeting – April 2000 •Meeting on Methamphetamine and MDMA Neuropharmacology – July 2001
Notice for Administrative Supplements for Post-Doctoral Research Training in Genetics – March 2001	Increasing Nursing Post-Doctoral Opportunities in Rare Diseases – May 2000
PA, Xenobiotecs & Cell Injury in Neurodegenerative Disease – 2001	Meeting on Xenobiotecs and Cell Injury in Neurodegnerative Disease
PA, Beryllium-Induced Disease – 2001	•Meetings in 1998 and September 2001 •Special on 20/20 highlighted Chronic Berylium Disease and research efforts
RFA, Developmental Toxicology Exploratory Grants – 2001	Government/Private Sector Consortium Meetings Held in 2000 and 2001
RFA, Role of Hormones in Prostate Cancer – 2001	Meetings on Hormones in Prostate Cancer – 2001
RFA, Autism Research Centers of Excellence – 2001	Meetings on Autism Research – 2000 and 2001

Research Goal B: Develop New or Improved Instruments and Technologies for Use in Research and Medicine	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
RFP, Data Coordinating for the Osteoarthritis Initiative – July 2001	Steering Group on The Osteoarthritis Initiative A Public/Private Research Collaboration – February 2000
RFP, Clinical Centers for the Osteoarthritis Initiative – July 2001	Steering Group on The Osteoarthritis Initiative A Public/Private Research Collaboration – February 2000
RFA, Gene Therapy for Neurological Disorders – September 2001	Gene Therapy for Neurological Disorders – October 2000
RFA, Mechanisms of Action of Deep Brain Stimulation – July 2001	•Deep Brain Stimulation for Parkinson's Disease Working Group – March 1999 •Parkinson's Disease Research Agenda – March 20000 •Therapeutic Opportunities for Parkinson's Disease – October 2000
RFA, Technology Development for Safe and Effective Deep Brain Stimulation – July 2001	•Deep Brain Stimulation for Parkinson's Disease Working Group – March 1999 •Parkinson's Disease Research Agenda – March 20000 •Therapeutic Opportunities for Parkinson's Disease – October 2000
RFA, International Clinical, Operational, and Health Services Research and Training Award – February 2001	NIH and Outside Expert Consultation Meeting – December 2000
RFA, Development of PET and SPECT Ligands for Brain Imaging (Phased Innovation Award) – September 2001	•Consortium for the Development of Novel PET and SPECT Lignads for Brain Imaging – January 2001 •Biomarkers and Surrogate Endpoints – April 1999
RFP, Speech Processors for Auditory Prostheses – February 2001	International Conference on Implantable Auditory Prostheses – August 1999
Notice, Biomedical Imaging Research Network: Notice of Limited Competition – March 2001	Biomedical Informatics Research Network Workshop – February 2001
PA, Extramural Research Facilities Improvement Program – August 2001	Research Facilities Improvement Program Workshop Summary – July 2001
RFA, Exposure Assessment Methods for Cancer Research – December 2000	Workshop on "The Role of Human Exposure Assessment in the Prevention of Environmental Disease" – September 1999
•PA, Development of Novel Technologies for In Vivo Imaging (Phased Innovation Award) – May 2001 •PA, Development of Novel Technologies for In Vivo Imaging (SBIR/STTR) – May 2001	•Imaging Sciences Working Group – July 1997 •Lung Imaging Workshop: Technology Transfer – January 1997 •Computer Aided Diagnosis and 3D Image Analysis – October 1998 •Quantitative In-Vivo functional Imaging in Oncology – January 1999 •Focus Group on Magnetic Resonance Spectroscopy in Clinical Oncology – April 1999 •Bioengineering Consortium Symposium – June 1999
PA, Design, Measurement, and Statistical Analysis in Mental Health Research – November 2000	Clinical Treatment and Services Research Workgroup Meetings: Bridging Science to Service – 1999
RFA, Health and Developmental Consequences of Prenatal Exposure to Methamphetamines – January 2001	•Early Environmental Stress and Biological Vulnerability to Drug Abuse – September 1999

Research Goal B: Develop New or Improved Instruments and Technologies for Use in Research and Medicine	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
	•Effects of in utero Exposure to Methamphetamines – March 2000 •Towards Neuroimaging Assessment of Early Drug Exposure – May 2000
PA, Drug Abuse Health Services Research – May 2001	Drug Abuse Health Services Research – June 1999

Research Goal C: Develop New or Improved Approaches for Preventing or Delaying the Onset or Progression of Disease and Disability	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
RFA, Institutional Pathways Towards Strengthening HIV Prevention in Minority Communities – September 2001	Planning Meeting for Issuing an RFA on Institutions and HIV Risk – April 2001
PA, The Role of Antioxidants in the Prevention of Diabetic Complications – June 2001	Workshop on Genetics of Diabetic Retinopathy – September 2000
PA, Translational Research for the Prevention and Control of Diabetes – April 2001	Workshop on Genetics of Diabetic Retinopathy – September 2000
RFA, Parkinson's Disease Neuroprotection Clinical Trial: Coordinating and Statistical Centers – February 2001	•Parkinson's Disease Research Agenda – March 2000 •Therapeutic Opportunities for Parkinson's Disease – October 2000
RFA, Parkinson's Disease Neuroprotection Clinical Trial – July 2001	•Parkinson's Disease Research Agenda – March 2000 •Therapeutic Opportunities for Parkinson's Disease – October 2000
RFA, Research Collaborations to Provide 900 MHz NMR Spectroscopy – June 2001	Experimental NMR Conference – April 2000
RFA, Centers of Excellence in Chemical Methodologies and Library Development – June 2001	Needs and Opportunities in Chemical Methodology and Library Development – August 2000
RFA, New Approaches to Prevent Hypoglycemia in Patients with Diabetes – July 2001	Workshop on Hypoglycemia and the Brain – September 2000
RFA, Understanding Hypoglycemia Unawareness in Patients with Diabetes – July 2001	Workshop on Hypoglycemia and the Brain – September 2000
RFA, Prevention and Treatment of Type 2 Diabetes in Children and Adolescents, Clinical Centers – October 2000	•Diabetes Mellitus Interagency Coordinating Committee meeting on Type 2 in Children – July 1999 •Diabetes Mellitus Interagency Coordinating Committee meeting on Type 2 in Native Americans with Focus on Children – May 2000
RFA, Prospective Cohort Study of Chronic Renal Insufficiency – September 2000	The Epidemiology of Chronic Renal Insufficiency – September 1999
RFA, Prevention of Alcohol-Related Problems Among Adolescents – October 2000	National Advisory Council Working Group on Research Priorities – March 2000
RFA, Research on High Alcohol Content Malt Beverages and Related Products – January 2001	•National Advisory Council Working Group on Research Priorities – March 2000 •Fortified Alcoholic Beverages Research Initiation Workshop

Research Goal C: Develop New or Improved Approaches for Preventing or Delaying the Onset or Progression of Disease and Disability	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
	– May 2000
PA, Cancer Prevention, Control, Behavioral and Population Sciences Career Development Award – September 2001	•Cancer Control Review Group – August 1997 •Cancer Prevention Program Review Group – June 1997
RFA, Centers of Excellence in Cancer Communications Research – February 2001	Ensuring Quality Cancer Care, National Cancer Policy Board, Institute of Medicine, and National Research Council – 1999
RFA, Research in State and Community Tobacco Control Interventions – October 2000	Tobacco Research Implementation Group – November 1998
RFA, International Initiatives to Prevent HIV/STD Infection – October 2000	Research Center and Program Project Directors Meeting – September 2000
RFA, Community Implementation of HIV Prevention Intervention – February 2001	HIV/AIDS: Bridging the Gap Between Research and Prevention in Communities – October 200
RFA, Malaria Vaccine Development: Understanding Malarial Anemia – January 2001	International Workshop on the Pathogenesis of Malarial Anemia – May 2000
RFA, Response to Presidential Vaccine Initiative: Overcoming the Tuberculosis Latency Challenge – March 2001	•International Workshop on the Pathogenesis of Malarial Anemia – May 2000 •Addressing the Presidential Challenge – May 2000
RFP, Millennium Vaccine Initiative: Novel Vaccines for Malaria and Tuberculosis – May 2001	Addressing the Presidential Challenge – May 2000
RFA, The Next Generation of Drug Abuse Prevention Research – January 2001	•Symposium and Forum on Building a Prevention Research Career: Pathways to Success – June 1999 •Assessing the Impact of Childhood Interventions on Subsequent Drug Abuse – May 2000 •Bridging Neurobiological, Behavioral, and Prevention Sciences – November 2000
RFA, International Studies on Drug Abuse and HIV/AIDS – January 2001	•Integrating HIV/AIDS Treatment into Drug Abuse Treatment – March 1999 •Drug Abuse and AIDS: Intertwined Epidemics – July 1999 •International Meeting on the Prevention of HIV in Drug Using Populations – August 1999
Funded seven Administrative Supplements to existing P30 Centers or currently funded R01 projects to pilot consortia/subcontracts to develop partnerships between majority and minority institutions – April 2001	Building Capacity for Nursing Research in Health Disparities – February 2001

Research Goal D: Develop New or Improved Methods for Diagnosing Disease and Disability	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
RFA, Microarray Centers for Research on the Nervous System – February 2001	Institute Strategic Plan: Neuroscience at the New Millennium – August 1999
PA, Metals in Medicine – March 2001	Metals in Medicine: Targets, Diagnostics, and Therapeutics – June 2000

Research Goal D:	***Develop New or Improved Methods for Diagnosing Disease and Disability***
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
RFA, Barrett's Esophagus, Gastrointestinal Reflux Disease and Adenocarcinoma of the Esophagus – July 2001	Series of Focused Research Workshops on Barrett's Esophagus – February-April 2001
RFA, Novel Biomarkers of Chronic Obstructive Pulmonary Disease – July 2001	Conference on Biomarkers and Surrogate Endpoints: Advancing Clinical Research and Applications – April 1999
PA, Genetic Testing and the Clinical Management of Nonsyndromic Hereditary Hearing Impairment – December 2000	•Working Group on Consideration for Developing and Implementing Genetic Diagnostic Tests for Hereditary Hearing Impairment and Other Communication Disorders – December 1998 •Third Workshop of the Working Group on Early Identification of Hearing Impairment – September 2000
RFA, Therapeutic Community Research – February 2001	•Drugs in the Workplace: Planning the Research Agenda – March 1999 •Drug Abuse Treatment in the Correctional Setting – March 2000 •Treating the Multiple Drug Abuser: Science-based Approaches – April 2000 •New Directions in Therapeutic Communities Research – August 2000
RFA, HIV/AIDS and Drug Use Among Adolescents – January 2001	•Integrating HIV/AIDS Treatment into Drug Abuse Treatment – March 1999 •Drug Abuse and AIDS: Intertwined Epidemics – July 1999 •International Meeting on the Prevention of HIV in Drug Using Populations – August 1999 •Synaptic Plasticity in Addiction and Other Changes in Behavior – October 1999 •HIV Prevention in Drug Using Populations – January 2000
RFA, The Transition from Drug Use and Addiction: Unearthing the Switch – November 2000	•Motives for Behavior: From Neurological to Cognitive Perspectives – June 1999 •Genetics and Drug Addiction – August 1999 •Introceptive Drug Cues: Beyond Drug Discrimination – August 1999 •Synaptic Plasticity in Addiction and Other Changes in Behavior – October 1999 •Brain Mechanisms Underlying Sleep and Drug Addiction – October 1999 •Cognitive Neuroscience and Drug Addiction: Primed for Interaction – April 2000 •Transitions to Addiction Symposium – April 2000

Research Goal E: Develop New or Improved Methods for Treating Disease and Disability	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
PA, Therapeutic and Pathogenic Approaches for the Muscular Dystrophies – January 2001	Therapeutic Approaches for Duchenne Muscular Dystrophy – May 2000
RFA, Clinical Trial Planning Grants to Guide Timing, Intensity, and Duration of Rehabilitation for Stroke and Hip Fracture – September 2001	Hip Fracture and Stroke Conference – August 2000
RFA, Diabetic Macular Edema Clinical Research Network – June 2001	Workshop on Genetics of Diabetic Retinopathy – September 2000
RFA, High Throughput Drug Screening Facility for Neurodegenerative Disease: Request for Information – January 2001	•High-Throughput Screening of Therapeutic Drug Candidates for ALS – April 2000 •Parkinson's Disease Research Agenda – March 2000
RFA, Administrative Supplements: FDA- Approved Compound Screens (with Huntington's Disease Society of America, The ALS Association, The Hereditary Disease Foundation) – May 2001	•High-Throughput Screening of Therapeutic Drug Candidates for ALS – April 2000 •Parkinson's Disease Research Agenda – March 2000
RFA, Ecology of Infectious Diseases – February 2001	Workshop on Ecology of Infectious Diseases – April 1999
RFA, Adult to Adult Living Donor Liver Transplantation Cohort Study – July 2001	Workshop on Living Donor Liver Transplantation – December 2000
PA, Functional Tissue Engineering for Heart, Vascular, Lung, Blood, and Sleep Disorders and Diseases: SBIR/STTR Initiative – October 2000	•SPARK Working Group – September 1998 •Tissue/Organogenesis Interest Group – November 1998
RFA, Stem Cell Plasticity in Hematopoietic and Non-Hematopoietic Tissue – November 2000	Working Group on Stem Cell Plasticity – March 2000
RFA, Overcoming Barriers to Treatment Adherence in Minorities and Persons Living in Poverty – January 2001	•Working Group on Adherence to Medical and Lifestyle Interventions – July 1999 •Conference on Behavioral Science Research and Diabetes – July 2000
RFA, Development of Innovative Treatment Approaches to Autism – December 2000	Workshop on Treatment of Autism – November 1999
PA, Adoption of Alcohol Research Findings in Clinical Practice – February 2001	National Advisory Council Working Group on Research Priorities – March 2000
RFA, Complementary/Alternative Medicine at the End of Life for Cancer and/or HIV/AIDS – January 2001	•Forum on "The End of Our Lives: Guiding the Research Agenda" – November 2000 •Research Workshop on Symptoms in Terminal Illness – September 1997
RFA, Developing Translational Research in Behavioral Science – November 2000	Behavioral Science Workgroup Meetings: Translating Behavioral Science into Action – 2000
PA, Translational Research Centers in Behavioral Science – December 2000	Behavioral Science Workgroup Meetings: Translating Behavioral Science into Action – 2000
PA, Collaborative R01s for Clinical and Services Studies of Mental Disorders and AIDS – July 2001	Clinical Treatment and Services Research Workgroup Meetings: Bridging Science to Service – 1999
PA, Developing Centers for Services and Interventions Research – May 2001	Clinical Treatment and Services Research Workgroup Meetings: Bridging Science to Service – 1999
PA, Mechanisms for Time-Sensitive Research Opportunities	Clinical Treatment and Services Research Workgroup

Research Goal E: Develop New or Improved Methods for Treating Disease and Disability	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
– September 2001	Meetings: Bridging Science to Service – 1999
PA, Effectiveness, Practice and Implementation in Children's Mental Health Services at Children's Service Sites – September 2001	Child and Adolescent Mental Health Services Research Planning Meeting – January 1999
RFA, EDTA Chelation Therapy for Coronary Artery Disease – April 2001	Conference on Complementary and Alternative Medicine in Cardiovascular, Lung, and Blood Research – June 2000
RFP, Intravenous Magnesium for Treating Acute, Severe Asthma Exacerbations – April 2001	Workshop on Magnesium Treatment for Severe, Acute Asthma: Assessment of State of the Science and Recommendations for Research – September 2000
PA, Therapeutic Research on AIDS-Associated Opportunistic Infections and Malignancies – June 2001	•Opportunistic Infections Working Group – January 1999 •Office of AIDS Research Planning Workshop – February 2000
RFP, Inner-City Asthma Consortium: Immunologic Approaches to Reduce Asthma Severity – June 2001	Expert Panel convened to review Extramural Asthma and Allergy Research Program – February, 2000
Four RFPs on Drug Development for Opportunistic Infections: *Mycobacterium Avium*, Pneumocystis Carinii, *Cryptosporidium Parvum*, *Cryptococcus Neoformans* – July 2001	•Office of AIDS Research Planning Workshop – February 2000 •AIDS Research Advisory Committee – September 2000
RFP, Drug Development for Opportunistic Infections: Hepatitis C – August 2001	•Symposium on Hepatitis C Framework for Progress – April 2000 •AIDS Research Advisory Committee – September 2000 •Office of AIDS Research Planning Committee – February 2001
PA, Therapeutic Research on AIDS-Associated Opportunistic Infections and Malignancies – June 2001	•Opportunistic Infections Working Group – January 1999 •Office of AIDS Research Planning Workshop – February 2000
PA, Drug Abuse Aspects of HIV/AIDS and Other Infections – November 2000	•Integrating HIV/AIDS Treatment into Drug Abuse Treatment – March 1999 •Drug Abuse and AIDS: Intertwined Epidemics – July 1999 •International Meeting on the Prevention of HIV in Drug Using Populations – August 1999 •HIV Prevention in Drug Using Populations – January 2000 •Females and Cocaine-HIV Interactions in the Central Nervous System – June 2000
Informal Caregiving Research for Chronic Conditions – 2001	Research in Informal Caregiving: State of the Science – July 2001

Research Goal F: Develop Critical Genomic Resources Including the DNA Sequences of the Human Genome and the Genomes of Improtant Model Organisms and the Disease-causing Microorganisms	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
RFA, Developing the Potential of Xenopus tropicalis as a Genetic Model – January 2001	Non-Mammalian Model Workshop – February 1999

PA, Development of Zebrafish Mutagenesis and Screening Tools – March 2001	•Genomic and Genetic Tools for the Zebrafish – May 1999 •Functional Genomics Workshop – September 1999
Broad Agency Announcement, Proteomic Technologies – September 2001	Special Emphasis Panel on Proteomic Technologies – March 2001
RFP, Mouse Neuroscience Phenotyping and Distribution Center – June 2001	Setting Priorities for Phenotyping the Mouse Nervous System and Behavior – June 2000
RFA, BAC (Bacterial Artificial Chromosome) Library Production – April and June 2001	•Workshop on Nonhuman Primate Genomics – January 2001 •Internal Staff Discussions and Institute Advisory Council Approval
PA, Technologies for Closing DNA Sequence Gaps And Improving Methods for Obtaining the Sequence of Difficult-to-Sequence Regions – June 2000	Internal Staff Discussions, Discussions with Research Grantees, and Institute Advisory Council Approval

Research Goal G: Work Towards the President's Goal of Developing an AIDS Vaccine by 2007	
Title of RFA/PA/RFP or Brief Description of Follow-up Action in FY 2001	**Name of Workshop/Other Meeting Held to Solicit Public Input**
Several Clinical Grade Lots of Plasmid Vaccine Candidates were Produced (VRC SP Goal 1) – 2001	VRC Strategic Plan – issued Nov/Dec 2000; result of a series of advisory board meetings, followed by refinement during meetings of VRC principal investigators
Clinical Grade Lots of Plasmid Vaccine Candidates (above) Advanced into Preclinical Evaluation (VRC SP Goal 2) – 2001	VRC Strategic Plan – issued Nov/Dec 2000; result of a series of advisory board meetings, followed by refinement during meetings of VRC principal investigators
Phase I Clinical Trial of a Gag/Pol DNA Vaccine Against HIV/AIDS Received Regulatory Approval (VRC SP Goal 3) – 2001	VRC Strategic Plan – issued Nov/Dec 2000; result of a series of advisory board meetings, followed by refinement during meetings of VRC principal investigators

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