

# National Institutes of Health



**Government Performance and Results Act**

**FY 2002 Annual Performance Plan,  
FY 2001 Final Annual Performance Plan, and  
FY 2000 Annual Performance Report**

**U.S. Department of Health and Human Services**

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# National Institutes of Health

## FY 2002 Annual Performance Plan, FY 2001 Final Annual Performance Plan, and FY 2000 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, the National Institute of Health's (NIH) Annual Plan and Annual Report materials are integrated into a single document, to eliminate redundancy and to facilitate presentation of the overall thrust of the agencies program strategies and accomplishments across multiple years.

This combined Annual Plan and Annual Report presents a four fiscal year picture, spanning FY 1999-FY 2002, of program plans, performance expectations, and accomplishments.

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 achievement of these goals. The goals and targets described for FY 2002 are "initial." The previously published "final" FY 2001 goals and targets are also included. (Any "revised final" FY 2001 goals and targets are explicitly noted as such.)

The reporting elements of this document describe NIH's accomplishments and progress toward goal achievement for each goal and target active in FY 2000. The assessment process compares the actual level of achievement in FY 2000 with that targeted. Where a goal spans several fiscal years of activity, the significance of the accomplishments in both FY 2000 and FY 1999 for overall goal achievement are discussed.

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# 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, the 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.

The NIH invests the public's resources and support for medical science in three basic and interrelated ways. First and foremost, the 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.

The 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

The 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. The 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 the 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, the 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 the 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. Research proposals are submitted to the NIH by scientists working at universities, medical, dental, nursing and pharmacy schools, schools of public health, non-profit research foundations, and private industry. 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 which are awarded to non-profit and commercial organizations for work requested and overseen by the 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.*** The 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 the 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.*** The 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, the 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.*** The 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. The 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.*** The 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. The 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.*** The 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 the 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 the 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 2002 President's budget request provides funding to support NIH staff (i.e., Full Time Equivalents), including approximately 2,000 intramural scientists, funding to support research efforts from a pool of extramural scientists, and funding to support the facilities (i.e., universities, research centers and the buildings on the NIH campus) necessary in the conduct of science. The combination of dollars, human capital, and physical facilities available for research make up the resources by which NIH accomplishes its program performance goals.

The dollar resources are distributed to NIH's programs through budget mechanisms that direct the funding to intramural and extramural researchers, contractors, NIH staff, universities and research centers. Ultimately, all funds are used to support NIH's mission and long-term goals.

NIH's highest priority is the funding of biomedical research. Funding is provided to the Research Program through a variety of budget mechanisms that includes: Research Project Grants (RPGs), Research Centers, Other Research, R&D Contracts, Intramural Research, Research Management and Support, Cancer Control, Library of Medicine and Office of the Director. RPGs are the major mechanism for this support. The emphasis on RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities.

NIH continues to be a leader in the training of biomedical and behavioral researchers. 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. Funds are provided to this program through the Research Training, Other Research, Research Management and Support, and Office of the Director mechanisms. NIH provides facilities support for the NIH campus and to universities and research centers by providing funds through the Buildings and Facilities, Construction, Research Management and Support, and Office of the Director mechanisms.

Under NIH's aggregated approach, performance goals are grouped under the three NIH Core Programs: Research, Research Training and Career Development, and Research Facilities. Within these three program areas, NIH has defined a crosswalk for how each budget mechanism (e.g., Research Project Grant, Research Management and Support, Construction, etc.) links to the three core programs. Further information on NIH budget policy can be found in the NIH FY 2002 Congressional Justification.

Resources	Budget Mechanisms	Core Program	Program Areas
\$23 Billion estimated for FY 2002  NIH Staff  Extramural Scientists  Contractors  Universities, Research Centers and NIH Facilities	<ul style="list-style-type: none"> <li>• Research Project Grants</li> <li>• Research Centers</li> <li>• Other Research</li> <li>• Research Training</li> <li>• R&amp;D Contracts</li> <li>• Intramural Research</li> <li>• Research Management and Support</li> <li>• Cancer Control</li> <li>• Construction</li> <li>• Library of Medicine</li> <li>• Office of the Director</li> <li>• Buildings and Facilities</li> </ul>	Research	Research
			Communication of Results
			Technology Transfer
			Research Leadership and Administration
		Research Training and Career Development	Training Support and Outreach
		Research Facilities	Intramural Modernization and Maintenance
			Extramural Assistance

## 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.

An example of NIH's partnership with extramural researchers that goes beyond the awarding of grants and contracts can be seen in NIH's current activities in the *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 the NIH's sister agencies in HHS, 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:

- ❑ *Human Genome Project.* NIH is currently working with the Department of Energy (and with other international collaborators) on the major effort to sequence the large and complex human genome. This endeavor is widely regarded as the single most important project currently in biology and biomedical science.
- ❑ *DNA Polymorphism Discovery Resource.* In one of numerous related studies, NIH worked recently with CDC and several independent scientists to assemble DNA samples from several hundred U.S. residents with ancestry from all the major regions of the world. This material will provide a resource of immense value for identifying human genetic variations, through which other studies can seek to relate to health and disease.
- ❑ *National Emphysema Treatment Trial.* NIH is collaborating with the Health Care Financing Administration (HCFA) and the AHRQ in a multi-center clinical trial designed to determine the role, safety, and effectiveness of bilateral lung volume reduction surgery in the treatment of emphysema.
- ❑ *Managing Pfiesteria and other harmful algal blooms.* NIH has worked collaboratively with a number of major federal agencies – National Oceanic and Atmospheric Administration (NOAA), Environmental Protection Agency (EPA), CDC, U.S. Department of Agriculture (USDA), Department of the Interior (DOI), and Food and Drug Administration (FDA) -- to develop a coordinated research strategy to identify ways to manage the health and environmental threats associated with *Pfiesteria* and other harmful algal blooms.

## Relationships with Private Industry

NIH also works with private industry in a number of ways, where there are opportunities to further NIH's research mission and to facilitate the flow of new biomedical knowledge and technologies to the private sector for further development and commercialization.

Among the various kinds of relationships possible, direct collaboration on research projects -- such as in the areas of vaccines, medical imaging, or other diagnostic tools -- is one important approach. Another is NIH's substantial efforts to facilitate the transfer of publicly funded research findings and technologies to the private sector. Additionally, NIH undertakes clinical

trials on new drugs and therapies that may have considerable commercial interest to the private sector.

Some examples of these relationships with the private sector include:

- ❑ *Vaccine research and development.* Most currently available vaccines, as well as those in the development pipeline, have resulted from collaborations between partners in the public and private sector, including federal and state governments, small and large corporations, academic research institutions and non-governmental organizations.
- ❑ *Technology Transfer through Cooperative Research and Development Agreements (CRADAs).* CRADAs are one major technology transfer mechanism used by NIH to enable private companies to work collaboratively with federal laboratory scientists and technologists in activities with the promise of yielding new technologies. (The CRADA mechanism was established by the Congress in 1986.)
- ❑ *Clinical Trials.* For example, NIH conducted a Phase I/II trial of recombinant methionyl human stem cell factor in patients diagnosed with acquired aplastic anemia. This trial was sponsored by Amgen, Inc., the private industry producer of the recombinant methionyl human stem cell factor.

## 1.4 Summary FY 2000 Performance Report

NIH reported on all of its 44 goals for FY 2000. 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 Web site).

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 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.

A comprehensive discussion on NIH's approach to performance assessment can be found in Appendix 2.



## Research

NIH's ongoing scientific enterprise 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 principal intended outcomes over the longer-term of these research activities are increased understanding of normal and abnormal biological functions and behavior and improved prevention, diagnosis, and treatment of diseases and disabilities. 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.

In October 2000, 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 met and assessed an illustrative sample of close to 600 FY 2000 Science Advances, Science Capsules, Stories of Discovery, and Research Awards/Honors that resulted from NIH funded research. (See Appendix 1). The results of this assessment are presented for the five research goals presented in Section 2.1.2.2 (Research) of this document. The independent Assessment Working Group concluded that NIH had substantially exceeded its five qualitative research goals.

Significant achievements and progress in FY 2000 include:

- New understandings of biological and behavioral processes, yielding answers to long-standing, important biological and behavioral questions, with the potential for translation into new or improved technologies, diagnostics, treatments, and preventive strategies.
- Enhanced knowledge about the 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.
- Better understanding of the contribution of biomedical in declines in disability in older Americans. Data from the National Long Term Care Survey continues to show that chronic disability rates are declining at an accelerating pace. Advances in biotechnologies attributed to behavioral changes, regaining of function, postponing the onset of disability, and reduction in the rate of degenerative processes of aging.
- Developed new diagnostic assays that open possibilities for better detection or more accurate predictions. For example, the identification of genetic markers in many studies can have an impact on other diseases and even other areas of research, as improved understanding of mechanisms of disease unfold from the genetic information.
- Generated new understandings about the mechanisms of serious nervous system disorders. Two mediators of the immune system, known as chemokines, were found to play key roles in

the inflammation of nerve cells in multiple sclerosis patients. A new mouse model of a serious inherited nervous system disorder known as neurofibromatosis was developed to help investigators identify the specific type of nerve cells that are damaged.

- Extended genomic sequencing to other organisms that serve important roles in biomedical research. The fruit fly and roundworm genetic sequences were recently completed, and they enhance investigators' use of these animal models in gaining key insights into cancer and aging mechanisms. Sequencing of the genomes from harmful bacteria and viruses is now aiding in our understanding of serious infectious diseases by providing investigators with new targets for vaccines, antiviral and antibiotic therapies, and have implications for addressing emerging infections, fighting bioterrorism, and antimicrobial resistance.
- 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.
- Announced, in June 2000, that the Human Genome Project public consortium had assembled a working draft of the sequence of the human genome. This was a seminal achievement for biology and biomedical research.
- Continued progress toward development of a vaccine for the HIV/AIDS by 2007. Diverse approaches to HIV vaccine design are being pursued – HIV envelope protein; DNA vaccines; candidate vaccines using functional proteins in addition to structural proteins, combination vaccines, and vaccines that stimulate both components (antibody and cell mediated responses) of the immune system. In addition, more candidate vaccines are reaching the human clinical trial stage.

In addition, the NIH initiated new and continued existing proactive efforts in the area of science communications by undertaking activities to increase the awareness of its research results among health care providers; high risk, under-served, or affected publics; and the general public.

Significant achievements and progress in FY 2000 include:

- Making substantial progress toward the goal of increasing awareness of selected NIH-sponsored research among health professionals. NIH has established relationships with provider organizations; identified most effective ways to communicate to health professionals; funded new demonstration projects to improve access to NIH medical treatment information; and developed information products for health professionals.
- Accelerating efforts to reach out to high risk, underserved, and other affected populations with intensified health education programs. These populations include older Americans, persons with low literacy skills, and minority populations.

- Ensuring that the public is fully informed about relevant research findings. NIH has accelerated efforts to communicate through the Internet, form partnerships with other organizations, and establish a dialogue with the media. These efforts have expanded NIH's capacity to reach broader numbers of people.
- Developed, among several ongoing activities related to the transfer of NIH-developed technology, a well-regarded, Web-based training module to better train the agency's scientists about technology transfer issues and options.

## **Research Training and Career Development**

One of NIH's important roles is 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 various types of grants and career development programs. These 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 the society's needs for health-related researchers. NIH's training and career development programs are also designed to enhance the quality and diversity of the biomedical research labor force.

Significant achievements and progress in FY 2000 include:

- Sustaining historical rates of application submission and awards in its major training programs (fellowships and career awards for basic scientists, research training grants, and entry level career awards). These statistics indicate that both the kinds of awards NIH offers remain popular with the pool of potential applicants and the quality of applications remains stable.
- Continuing the progress made over the last two years in awarding training grants to strengthen the pool of clinical researchers trained to conduct patient oriented research to help ensure that it is at or exceeds the targeted performance levels.
- Completing a detailed report on the early careers of predoctoral trainees and fellows supported by National Research Service Awards (one of NIH's most important training support programs), as part of a larger effort to better measure and effectively manage training and career development programs at the NIH.

## **Research Facilities**

NIH's Research Facilities Program takes on two broad tasks: a) supporting the construction, renovation, and maintenance of NIH 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 achievements and progress in FY 2000 include:

- Completing construction for the Dale and Betty Bumpers Vaccine Research Center (VRC). The VRC is a five story, consolidated facility to support all aspects of vaccine research.
- Continuing progress on the Louis Stokes Laboratory (LSL) to the 90% construction phase with expected completion in FY 2001. LSL is a six story, consolidated research facility that will replace existing obsolete laboratory facilities on the Bethesda Campus and will be used by a number of NIH's Institutes and Centers.
- Continuing substantial progress on the five year project to construct the Mark O. Hatfield Clinical Research Center (CRC) – still on schedule to be completed in FY 2003. The CRC will become a new heart of NIH's intramural research program, providing a 250 bed research hospital, allied clinical facilities, and adjacent laboratories.
- Keeping on track other major construction projects on the Bethesda campus that now in early stages of development, including revitalization of the Warren Grant Magnuson Clinical Center (design work to start in FY 2002), the Central Vivarium/Animal Research Center (design work to be completed in FY 2002), and the John Edward Porter Neuroscience Research Center (construction to start in FY 2002).
- Playing a critical role in reviewing and approving construction designs of grantees' proposals as related to the award of grants to the extramural research community to support the construction and modernization of research facilities. (Funding does not go forward without such approval.) While this process can be complex and time consuming, NIH has been able to sustain a pace of approval that is substantially in line with its planned performance.

## Part II. Program Planning and Assessment

This part of the Annual Plan describes NIH's performance goals and targets for FY 2002 and FY 2001 (as revised). Performance assessment reporting on the FY 2000 goals is also integrated.

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. The performance goals for these Programs are subsequently divided according to the major functional areas involved.

A detailed description of the performance goals, along with a discussion of the performance measures and data which underlie assessment, is provided for each Program and functional area. Several kinds of summary charts placed in each of these sections overview the performance goals and assessment findings. Several appendices at the end of the document provide additional details on NIH activities, the agency's approach to GPRA, and other essential supporting information.

	<b>FY 2002 President's Budget Request</b> (dollars in thousands)			
	<b>FY 1999 Actual</b>	<b>FY 2000 Actual</b>	<b>FY 2001 Estimate</b>	<b>FY 2002 Estimate</b>
Research	\$14,580,705	\$16,692,719	\$19,024,773	\$21,487,959
Research Training and Career Development	811,120	912,241	1,032,697	1,131,739
Research Facilities	239,343	251,747	240,799	422,204
All Programs	\$15,631,168	\$17,856,707	\$20,298,269	\$23,041,902

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## 2.1 Research Program

<b>GPRA Research Program</b>				
<b>FY 2002 President's Budget Request</b> (dollars in thousands)	<b>FY 1999 Actual</b>	<b>FY 2000 Actual</b>	<b>FY 2001 Estimate</b>	<b>FY 2002 Estimate</b>
	<b>\$14,580,705</b>	<b>\$16,692,719</b>	<b>\$19,024,773</b>	<b>\$21,487,959</b>
<b>Major Functional Areas</b>	<p><b>Research</b> -- 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.</p>			
	<p><b>Communication of Results</b> -- Communicate scientific results and health information to the medical research community, health care providers, patients, and the general public.</p>			
	<p><b>Technology Transfer</b>-- 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.</p>			
	<p><b>Research Leadership and Administration</b></p> <p><i>Priority setting</i>—implementing decision making mechanisms and policies that ensure NIH research is responsive to emerging health needs, scientific opportunities, and new technologies.</p> <p><i>Grants administration and peer review</i>—maintaining effective and efficient grants administration and a high quality of peer review to ensure the most meritorious research projects are considered for funding.</p> <p><i>Agency management and administrative support</i>—ensuring that management and administrative functions necessary to support the agency's mission are carried out effectively and efficiently.</p>			

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## 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 earlier discussion in Part I), 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.

**Summary of Performance.** Comprehensive summary tables covering all the goals and targets in this program appear at the outset of each functional area discussion. Please refer to the following pages:

Research .....	24
Communication of Results .....	141
Technology Transfer .....	188
Research Leadership and Administrative Support	
Priority Setting .....	208
Grants Administration and Peer Review .....	208
Agency Management and Administrative Support .....	211

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

### 2.1.2.1 Research

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 commonalities. 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 Goals Summary Table – Research**

Performance Goal	Targets	Actual Performance	Details
<p><b>a) Add to the body of knowledge about normal and abnormal biological functions and behavior.</b></p>	<p><b>Annual Target</b> Progress in advancing scientific understanding in key fields bearing on our knowledge of biological functions and behavior in their normal and abnormal states.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially exceeded.</p> <p><b>FY 1999</b> Target substantially exceeded.</p>	<p>Page 29</p>
<p><b>b) Develop new or improved instruments and technologies for use in research and medicine.</b></p>	<p><b>Annual Target</b> Progress in developing new instrumentation or technologies that enhance capabilities for investigating biological functions and diagnosing and treating diseases and disorders.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially exceeded.</p> <p><b>FY 1999</b> Target substantially exceeded.</p>	<p>Page 66</p>
<p><b>c) Develop new or improved approaches for preventing or delaying the onset or progression of disease and disability.</b></p>	<p><b>Annual Target</b> 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.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially exceeded.</p> <p><b>FY 1999</b> Target successfully met.</p>	<p>Page 77</p>
<p><b>d) Develop new or improved methods for diagnosing disease and disability.</b></p>	<p><b>Annual Target</b> 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.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially exceeded.</p> <p><b>FY 1999</b> Target substantially exceeded.</p>	<p>Page 89</p>



Performance Goal	Targets	Actual Performance	Details
	<p>2. Finish one-third of human genome (accuracy of at least 99.99%).</p> <p>3. In collaboration with The SNPs Consortium (TSC), identify 750,000 single nucleotide polymorphisms (SNPs).</p> <p>4. Complete sequencing of five additional bacterial pathogens and five chromosomes of protozoan parasites.</p> <p>5. Augment existing knowledge of pathogen genomes by initiating sequencing projects for at least six additional genomes (bacterial, fungal, parasitic).</p> <p>6. Complete worldwide sequencing effort of the entire genome of Plasmodium falciparum.</p> <p><b>FY 2000</b></p> <p>1. 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.</p> <p>2. Finish the sequence of at least one human chromosome.</p> <p>3. Complete sequence of the genome of Drosophila melanogaster (excluding heterochromatin).</p> <p><b>FY 1999</b></p> <p>1. U.S. annual production rate of human genomic sequence: 90 million base-pairs.</p> <p>2. Worldwide annual production rate of human genomic sequence: 220</p>	<p><b>FY 2000</b></p> <p>Target met. The Human Genome Project public consortium completed a "working draft" of the sequence of the human genome.</p> <p>Target significantly exceeded. The Human Genome Project public consortium completed the "finished" sequence of two human chromosomes.</p> <p>Target met. A consortium of publicly funded scientists, in collaboration with a private company, published the genome sequence of the fruit fly (Drosophila melanogaster)</p> <p><b>FY 1999</b></p> <p>Target significantly exceeded. An annual U.S. production rate of 173 million base-pairs was achieved.</p> <p>Target significantly exceeded. An annual worldwide</p>	

Performance Goal	Targets	Actual Performance	Details
	<p>million base-pairs.</p> <p>3. Total human genomic sequence completed worldwide at the end of FY 1999: 400 million base-pairs.</p> <p>4. Complete the sequence of the C.elegans genome.</p>	<p>production rate of 265 million base-pairs was achieved.</p> <p>Target met. The worldwide completed sequence achieved was 442 million base-pairs.</p> <p>Target met. The complete sequence of the C. elegans genome was published in Dec. 1998</p>	
<p><b>g) Develop an AIDS vaccine by 2007.</b></p>	<p><b>FY 2002</b></p> <p>1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.</p> <p>2. Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.</p> <p>3. Progress in collaborating with scientists in developing countries and with industry to further promote the development of vaccines for world-wide use.</p> <p>4. Progress in (a) completion of ongoing trials and (b) 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.</p> <p><b>FY 2001</b></p> <p>1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.</p> <p>2. Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.</p> <p>3. Progress in collaborating with scientists in developing countries and with industry to further promote the development of vaccines for world-</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p>	<p>Page 126</p>

Performance Goal	Targets	Actual Performance	Details
	<p>wide use.</p> <p>4. Progress in (a) completion of ongoing trials and (b) 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.</p> <p><b>FY 2000</b></p> <p>1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.</p> <p>2. Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.</p> <p>3. Progress in collaborating with industry to enhance opportunities for vaccine development.</p> <p>4. Progress in (a) completion of ongoing trials and (b) initiation of additional trials of new or improved concepts and designs, including the progression of promising candidates to larger trials testing vaccine candidates.</p> <p><b>FY 1999</b></p> <p>1. Increases in the research portfolio supporting innovative vaccine discovery.</p> <p>2. Increased interactions between academic investigators and industry, to enhance opportunities for vaccine discovery and product development.</p> <p>3. Progress in completion of ongoing trials and initiation of additional trials of new vaccine concepts and designs.</p>	<p><b>FY 2000</b></p> <p>Target met. Notable progress was made both scientifically and programmatically.</p> <p>Target met. A variety of animal models were utilized to make important advances.</p> <p>Target met. HIV Vaccine Design and Development Team awards made in FY 2000 substantially promote university-industry collaboration.</p> <p>Target met. Three ongoing trials were completed and one new trial initiated.</p> <p><b>FY 1999</b></p> <p>Target met. The number and dollar value of awards made for vaccine discovery increased in FY 1999.</p> <p>Target met. Actions were taken to increase the interaction of academic investigators and industry.</p> <p>Target met. Four new trials were begun. And of the seven trials started in prior fiscal years, two were completed.</p>	



**Performance Goal Details - Research**

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

**Performance Targets & Results****Annual Target**

**Progress in advancing scientific understanding in key fields bearing on our knowledge of biological functions and behavior in their normal and abnormal states.**

*FY 2001-2002 performance to be reported in February 2002 and 2003, respectively.*

**FY 2000**

*Performance: Target substantially exceeded. 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.*

**FY 1999**

*Performance: Target substantially exceeded. 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.*

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

### ***Goal Background***

Scientific advances are generally incremental, and they build on previous discoveries. The importance of a particular discovery may not be immediately apparent. That is, its significance and impact on human health and quality of life may become evident only after years of continued research.

Even with the significant improvements in health care gained in the past 25 years, much of health care today involves treating the symptoms of disease without understanding the underlying causes and precise mechanisms by which disease develops. To effectively and systematically attack today's chronic diseases, e.g., cancer, heart disease, dementia, diabetes, addiction, mental illness, AIDS and other emerging infections, we need a broad base of knowledge about normal living systems. We need to understand how living systems operate at the most basic levels, for example, the structure and function of genes, proteins, conjugates of carbohydrates and fats with proteins, and at the most complex levels, how these molecules organize and function together as living units (cells, tissues, whole organisms, and communities). We also need to understand how disease, genetic alterations, and environmental factors affect functioning at these levels, and their consequences for human health.

Goal A encompasses both basic as well as some aspects of clinical research. The research encompassed within this goal is intended to expand our understanding of normal biological processes and how they malfunction in disease and disability. This knowledge provides the fundamental theories and concepts for more disease-oriented investigations that lead to new methods for diagnosing, treating, and preventing disease and disability.

### ***Performance Assessment Approach***

#### *Basis and Data:*

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

The Working Group developed its assessment based on data provided by the ICs (science advances, science capsules, stories of discovery, and research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. (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 by the Working Group in assessing the outcomes of NIH research under Goal A in FY 2000 follow:

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 apply:

- ❑ 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 agents is translated into new understanding of the role of genes and/or the 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 to biological functions and behavior, or new findings are not published/and or disseminated.

*Validation and Verification:*

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

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

Target substantially exceeded. The Working Group unanimously concluded that the research outcomes submitted for FY 2000 demonstrated that NIH had fulfilled the criteria (see *Performance Assessment Approach* above) for “substantially exceeding” the goal of adding to the body of knowledge about normal and abnormal biological functions and behavior.

NIH’s Institutes and Centers submitted 279 science advances, science capsules, and stories of discovery (tabulated at the end of this section) that, in their judgment, demonstrated progress in adding to the body of knowledge about normal and abnormal biological functions and behavior. These outcomes spanned a spectrum from genomics and molecular biology to studies of human populations and health care delivery. They included basic research that contributed to advances in all areas of clinical medicine and behavior.

## Research Outcomes and Their Significance

The Working Group congratulated the NIH for its role in the sequencing of the human genome and the genomes of several animal models, landmarks of extraordinary significance. The contribution of various genetic techniques to the understanding of all areas of biomedical research, ranging from basic biology to the development of preventive and the therapeutic measures for inherited and acquired diseases, was identified by the Working Group as particularly noteworthy. The Group highlighted technological developments that will permit the analysis of the activity of thousands of genes at once, and progress in understanding complex diseases caused by defects in more than one gene. In addition, the Group noted the essential role of animal models in the understanding of basic biological phenomena and diseases. Animal models are critical not only for comparative genomic analysis, but also because of the availability of genetic mutants, including “knockout” animals that lack a particular gene, and transgenic animals into which a gene has been introduced through the techniques of genetic engineering. And, of course, animal models are valuable because of the ability to conduct experiments on them that cannot be done on humans. Finally, a complementary theme emerged from the Group’s discussions. This was the role of environmental factors in shaping biological phenomena, particularly in concert with genetic factors.

The Working Group emphasized the importance of establishing and sustaining a robust body of knowledge about biological function and behavior because this knowledge is essential to understanding almost all translational and clinical research efforts. The importance of NIH-supported research to achieving this goal was discussed within the context of the several broad categories of biological/biomedical research.

### Genetics and Molecular Biology

The Working Group emphasized that this is a very exciting time at the intersection of genetics, cell biology, and medicine. The Group pointed out that the advances in this area provide vast opportunities to explain the molecular bases of a wide variety of human diseases. In the last year, genomics has advanced at a spectacular pace, principally as a result of the determination of the DNA sequences of the genomes of several organisms, including a draft of the human genome and complete sequences of two human chromosomes. These milestones were achieved through an international effort involving both the public and private sectors. The extraordinary implications of this effort for understanding disease and disability are suggested by the fact that of the two completely sequenced chromosomes, it is already known that genes on these chromosomes play a role Down’s syndrome, Alzheimer’s disease, manic-depression, schizophrenia, heart disease, and a number of birth defects and cancers. The Group also noted that the achievements of the Human Genome Project are being produced ahead of schedule and under budget.

*Sequencing of the Human Genome and the Genomes of Model Organisms.* The Working Group stressed that the sequencing of the genomes of animal models is critical to understanding the functional significance of the DNA code. In particular, as discussed in greater detail below, the sequence of the genome of the fruit fly, *Drosophila melanogaster*, will be extremely valuable because it has been a mainstay in understanding the role of genes in development. And the

sequences of even simpler organisms such as the bacterium (*Escherichia coli*), the yeast (*Saccharomyces cerevisiae*), and the roundworm (*Caenorhabditis elegans*), will also contribute a great deal to understanding cellular and molecular mechanisms. Indeed, an NIH-supported multicenter team has already found that many genes that are known to cause disease in humans, including genes that contribute to colon cancer, muscular dystrophy, and Parkinson's disease, have direct counterparts in yeast, worm, and fruit fly. Thus, the genomes of the model organisms provide great opportunities for understanding the biological function of human disease genes, which can't be readily accomplished by the direct study of humans.

The Group also noted that a working draft sequence of perhaps the most relevant animal model, the mouse, is imminent. The mouse is a closely related species to the human and has many of the same physiological properties. Indeed, both genomes contain approximately 50-100,000 genes, and the coding regions of the genomes of the two species are approximately 85% identical at the genetic level. The mouse model is also suitable for the study of many human diseases, including Huntington's disease, and blood disorders such as acute myeloid leukemia. Finally, the mouse is particularly valuable because many strains bearing specific genetic mutations are available, and modern technology allows researchers to delete ("knockout") specific genes. This type of experimental manipulation is a powerful tool for deciphering the function of genes and their contributions to human disease. "Knockout mice" have revealed critical information in a broad variety of areas, such as immune deficiency, appetite and body mass, polycystic kidney disease, alcoholism, and diabetes.

In addition to the general impact and implications of the sequencing of the human genome and the genomes of model organisms, the Working Group focused on advances in five key areas stemming from the explosion of knowledge about genetics. These areas are the use of microarrays to analyze human disease; the determination of the genetic bases of many rare, inherited diseases; advances in the understanding of complex, multifactorial inherited disorders; insights into the regulation of gene expression; and the development of the field of pharmacogenomics, which is the study of genetic variation in response to drugs and other chemicals.

*Microarray Technology.* The Working Group noted that with comprehensive knowledge about the genes within the genomes, scientists are able for the first time to comprehensively monitor the expression of genes in any cell or tissue of interest. Scientists can now study the patterns of expression of thousands of genes through the use of microarray high density "chips." This powerful technology has qualitatively changed the types of analyses that can be performed. One very exciting example of the use of microarrays is the analysis of melanomas in both human and mouse to determine whether the tumors have metastatic potential. Most cancer deaths are due to metastasis, when cancerous cells spread to organs distant from the primary site of disease and grow into new tumors. Using microarray technology, NIH-funded scientists identified a gene that causes noninvasive, poorly metastatic melanoma cells to become metastatic. Identification of this gene, rhoC, provides an opportunity to develop diagnostic tests for metastatic tumors, as well as strategies to block metastasis. The Group also noted the profound implications of two other studies that used microarray technology. In one, scientists identified molecular differences between curable and incurable B-cell non-Hodgkin's lymphomas, providing clues to the development of treatments for the latter cases. In another, scientists identified molecular

signatures that are correlated with different prognoses for breast cancer. Studies of this type will be of increasing importance in understanding and treating a wide variety of human diseases.

*Rare Inherited Diseases.* Studies of rare inherited diseases not only reveal the genetic bases for these diseases, an essential step toward prevention or treatment, but also provide insight into basic cellular and molecular processes relevant to many human diseases and disorders. The Working Group identified a number of important advances in this area made during the last year. For example, NIH-supported scientists discovered a genetic abnormality associated with lymphangioleiomyomatosis (LAM), a rare and devastating lung disease characterized by the overgrowth of muscle-like cells in the lung. The normal form of the gene encodes a protein that suppresses tumor formation. This finding is relevant not only to the development of treatments for LAM, but also to certain related disorders and perhaps to the understanding and treatment of tumors in general. The applicability of findings from rare disorders to more common ones is also illustrated by an advance describing a link between a rare movement disorder, ataxia telangiectasia, and breast cancer. In that study, NIH-funded scientists showed that the gene that causes ataxia telangiectasia, and BRCA-1, a gene associated with breast cancer, are both involved in a biochemical pathway that allows cells to repair damaged DNA. Thus, this finding may not only explain why there is an increased risk of cancer among children with ataxia telangiectasia, but also help explain breast cancer. Similarly, scientists identified a gene that is frequently mutated in patients with Carney complex, a rare genetic disease that results in multiple tumors of the heart, skin, breast, nervous system, and endocrine glands. In addition, they found that the gene contributes to the composition of a protein that ordinarily acts as a tumor suppressor in most human cells. The identification of this gene therefore provides a clue to a biological mechanism underlying a variety of tumors, in addition to the mechanism in Carney complex. The possibility of broad applicability of the knowledge acquired in the study of a rare disease is not limited to the area of cancer research. For example, scientists found that patients with unusual inherited immunodeficiencies had a mutation that affected a protein critical to the functioning of antibody-producing cells. Subsequent studies showed that this protein is present in a variety of cell types in the immune system, suggesting that its role in the immune response may be broader than was previously thought. Clearly, studies of rare diseases often yield an unexpected dividend beyond the obvious value of the research to those who have the disease.

*Multifactorial Diseases.* In addition to these single gene disorders, a number of important multifactorial traits have been investigated and some of these have been mapped at the molecular level. In a few cases, potential disease-causing mutations have been identified. However, for these multifactorial traits, making this link is much more difficult and requires the integration of work by different investigators using different scientific approaches. Of particular interest, a new gene that may contribute to the pathogenesis of type 2 diabetes has been found—a surprising finding that might not have occurred without sophisticated gene mapping capabilities. Type 2 diabetes is recognized as a polygenic disease, meaning that multiple diabetes susceptibility genes may exist in the population at large and that multiple genetic determinants within a single individual may contribute to the disease. In addition to these genetic influences, environmental factors are also important contributors to the development of diabetes. Other studies have shown that susceptibility to multiple sclerosis may be inherited, but the genetics of this disorder are probably complex, involving several genes working in concert with

environmental factors. The complexity may reflect multiple susceptibility genes in a given individual (polygenic inheritance), different genes in different patients (locus heterogeneity), and possibly more than one underlying cause (etiological heterogeneity). Genes associated with prostate cancer and schizophrenia have also been mapped. Fully characterizing the genetic factors operating in these and other multifactorial disorders is an important goal that will be greatly facilitated by the sequencing of the human genome and animal models.

*Regulation of Gene Expression.* Gene expression is the process that generates the production of proteins as dictated by the genetic code. The expression of any gene must be closely regulated to provide the right amount of the gene product, which varies depending on tissue type, developmental stage, and other factors. The importance of appropriate regulation of gene expression is apparent from the fact that over expression of certain genes can lead to the development of tumors. The Working Group commented on the insights provided by one study that examined how in some cases, gene expression is limited to one of the two copies of the gene inherited from the mother and father, a phenomenon known as “imprinting.” When imprinting occurs, the expressed gene may be derived from either the mother or the father. In addition to providing new insight into some of the fundamental aspects of the regulation of gene expression, this has practical implications for gene therapy, by providing a means to overcome the problem of insufficient expression of a desired gene product.

*Pharmacogenomics.* Pharmacogenomics is the study of genetic variation in response to drugs and other extrinsic substances that the human organism encounters in the environment. The human genome comprises three billion deoxyribose nucleotides connected in two linear sequences in the chromosomes. The DNA sequences from any two persons are about 99.9% identical. There are single nucleotide differences between individuals in about 1/1000 base pairs. Whereas most of these differences do not have any effect, some single nucleotide polymorphisms (SNPs) can cause severe disease, as can differences in the lengths of certain repeated sequences, called microsatellites. Such differences also contribute to between-individual variation in responses to environmental agents that are normally not present in the human body, such as alcohol, nicotine, pharmaceutical compounds, and insecticides. A number of NIH-supported studies in the past year have indicated increasing awareness of this important area of research.

The Working Group noted that a study of genetic variation in the response to asthma treatment illustrates the value of pharmacogenomic information as a way of optimizing treatment according to genetic factors. Bronchodilator drugs called beta adrenergic agonists are ordinarily used to open asthma patients’ airways and keep them open. However, in some patients, regularly scheduled use of bronchodilators worsens airflow in the lungs. NIH-supported researchers found that this phenomenon was observed in patients with a specific genetic makeup, or genotype, that affects the structure of the  $\beta_2$  adrenergic receptor, a protein in the lungs that is responsible for the effect of the beta agonist drug. For these patients, beta agonists should be used on an “as needed” basis, rather than regularly scheduled, to maximize the effectiveness of the drug.

The Working Group also highlighted studies of the genetic factors and molecular mechanisms underlying an individual’s risk for alcoholism. Previously, scientists had shown that a person’s baseline sensitivity to alcohol is directly related to the risk of alcoholism, and that half the risk

for alcoholism is genetic. Scientists explored the molecular control of alcohol sensitivity in two animal models. Using the fruit fly, *Drosophila*, they found that mutations in several genes related to an intracellular signaling system (cAMP) increased the flies' sensitivity to alcohol. Then, using "knockout" mice, scientists showed that inactivation of another gene related to that intracellular signaling system made the mice resistant to alcohol's effects, leading them to drink more alcohol than normal mice. These studies provide clues as to the genes that might be involved in variations in sensitivity to alcohol and the risk of alcoholism in humans. Similarly, scientists have studied genetic variations in the responses of individuals to environmental contaminants. In one such study, scientists found that variations in a gene that codes for an enzyme that detoxifies certain insecticides could lead to major differences in an individual's sensitivity to particular insecticides. Studies of this type have significant implications for the assessment of individual risks from exposure to drugs or toxicants, as well as for safety testing of chemicals such as insecticides.

### Animal Models

Because all organisms are made of the same basic materials, and many share similar genetics and physiologic processes, researchers seeking to understand both normal and disease processes in humans can learn a great deal by studying similar systems in simpler "model organisms" such as worms, yeast, fruit flies, and rodents. Model systems have proven to be essential tools for understanding a wide array of human conditions, providing critical new insights into the molecular mechanisms leading to cardiovascular, gastrointestinal, neurological, structural, and other defects that may have counterparts in human disorders.

*Drosophila melanogaster*. The Working Group applauded an accomplishment this year that complements the description of the basic roadmap of the human genome—the near-completion of the genome sequence of the fruit fly, *Drosophila melanogaster*. In March of 2000, a consortium of publicly and privately funded institutions jointly announced that they had unscrambled the genome of this organism, with only 400 gaps remaining at that time. Completion of the entire sequence is anticipated in 2001. The fruit fly has been the centerpiece of experimental genetics in the past century, especially with regard to the genes that control development of body parts and organs. The importance of the fruit fly as a genetic model for human biology is that about 180 of the 290 human genes for which a mutation is known to cause disease in humans (i.e., about 60%) have direct counterparts in the fruit fly. A complete catalog of fly genes is, therefore, an extraordinary tool to study a variety of complex developmental and physiological processes, as well as in the production of disease. The study of gene-environment interactions is another compelling direction of research, in which the fruit fly may serve as an experimental model.

The fruit fly has certain advantages over the mouse and the rat, which are the principal animal models currently used to study physiology and behavior. The fruit fly life cycle is short, it requires less space for housing, and a variety of phenotypes can be screened in a high throughput fashion. For example, a recent study used ethyl methane sulfonate to produce flies that varied in their sensitivity to alcohol, a commonly encountered environmental substance for the fruit fly, owing to the fermentation of ripened fruit. From the 30,000 potential mutant flies generated, scientists isolated 19 strains with decreased sensitivity to the acute effects of alcohol,



and four with increased sensitivity. In addition to such random mutagenesis through the use of a chemical agent, the fruit fly can also be genetically manipulated by techniques used for the mouse, namely, through the development of transgenic, knockout and recombinant inbred animals.

Recent examples of how the fruit fly contributes to the understanding of human biology include studies on the genetic control of circadian rhythm (biological clock), hunger, central nervous system abnormalities associated with aging (e.g., Parkinson's disease) as well as aging itself, and memory and learning. Its use as a model of behavior in response to environmental conditions and agents is exemplified in recent studies on the response of the fruit fly to alcohol (see above discussion). Genes that impart increased and decreased sensitivity to alcohol's sedative-hypnotic effects have been identified and the pathways that mediate sensitivity to alcohol have been explored. Many of these studies, as well as others utilizing the fruit fly are discussed in greater detail below. The sequencing of the fruit fly genome will make it even more valuable for studying a wide variety of biological phenomena.

*Knockout and Transgenic Mice.* The Working Group also highlighted the impact of the development of "knockout" and transgenic mice on the understanding of human biology. Gene knockout is the process whereby a specific gene's function is eliminated. The impact of this genetic manipulation is assessed by studies of the animal's development, reproductive capability, behavior, physiology and anatomy. This process is called phenotyping. Transgenic manipulation is the process whereby a segment of a foreign DNA or gene is inserted into the genome of a host animal. The inserted DNA can be from a different animal species, e.g., human. The impact is again assessed by phenotyping. Recently, major advances have been made in developing reagents, genomic information, and critical germline modification techniques for the production of transgenic and knockout mice and rats. With these tools in place, experimental rodent models can make unprecedented contributions toward understanding the molecular basis of human health and disease. Thus far, the mouse has been the principal vertebrate animal model in such studies. A number of studies conducted by NIH-supported researchers (some of which are discussed in greater detail below) illustrate how this research approach has greatly increased our ability to study human gene function and mechanisms of disease.

### Cellular Growth and Differentiation

The Working Group highlighted a variety of advances in understanding the fundamental aspects of cell growth and differentiation, particularly those in the area of cancer. Many of these advances illustrate the power of genetic and molecular techniques to elucidate the biological bases of the uncontrolled growth of cancerous cells. Other studies emphasize the contributions of environmental and hereditary factors in the development of cancer. Finally, the Working Group discussed exciting new cancer therapies developed with NIH funding, and other studies that examined ethical and practical considerations in conducting clinical trials to evaluate new therapies.

*Genetic and Molecular Approaches to Understanding Cancer.* The Working Group highlighted several advances that contributed to the understanding of the means by which normal cells become cancerous. For example, several NIH-funded studies examined the role of normal cell

death, or apoptosis, in the development of cancer. These studies concluded that a particular protein (called survivin) that regulates apoptosis may be important in the development of cancer. The gene that codes for survivin is improperly regulated in cancerous tissue, and an excessive amount of it is produced. Because of the high concentration of survivin, cells that would ordinarily die may proliferate, causing a tumor to grow. Thus, survivin holds promise both as a marker of cancer progression and as a possible target for therapeutic intervention. If researchers can block the production of survivin, they may be able to develop a successful cancer therapy. Because of survivin's possible utility as a marker of cancer progression, these studies are also referenced in the section of this report that covers diagnosis.

The Working Group noted that the development of validated experimental animal models of human disease is critical to the understanding of cancer, including brain tumors. An example of a valuable contribution of this type was the development of a mouse model of neurofibromatosis, one of the most common genetic disorders of the nervous system. In the most common form of this disorder, neurofibromatosis 1 (NF1), patients develop multiple benign and malignant tumors (neurofibromas) along nerves. Although the genetic defect responsible for human NF1 has been known for nearly a decade, researchers succeeded in developing a mouse "knockout" model of the disorder only this year, because it was necessary to inactivate a second gene called *p53*, in addition to the *Nf1* gene, to produce malignant tumors in the mouse. Mice with only a defective *Nf1* gene can be made to develop the benign neurofibromas so common in human patients. These mouse models will contribute to the understanding of NF1, as well as the development of drugs that may block tumor development.

The Working Group also noted the extraordinary potential of microarray technology in cancer prognosis and pathology. The technology, discussed above, can be used to distinguish metastatic and non-metastatic cancers, and to determine whether certain cancers are likely to be curable.

*Environmental and Hereditary Contributions to Cancer.* The Working Group emphasized the importance to the public's understanding of cancer of an epidemiological study of the relative contributions of genetic and environmental factors to the risk of developing cancer. Using data on nearly 45,000 pairs of twins, the researchers assessed the risk of cancer at 28 locations on the body. Statistical modeling was used to determine the relative importance of heritable and environmental risk factors in causing cancer. Although the study found that hereditary factors increased the risk of certain cancers such as prostate, breast, and colorectal cancer, it concluded that the environment is the major contributor to the risk of developing these and most other cancers. Indeed, it showed that the probability that identical twins would develop cancer at the same anatomical location was no more than 10 percent. By contrast, the environmental contribution to cancer risk ranged from 58 to 82 percent. Accordingly, this study should relieve public anxiety about the inevitability of genetic effects on the development of cancer.

The Working Group also highlighted a molecular study that illustrates how environmental factors, such as cigarette smoke, contribute to the development of cancer through their effects on certain genes. The researchers examined secretions, or sputum, obtained from the lungs of patients with a form of lung cancer known as squamous cell carcinoma. The researchers studied the DNA in the sputum samples of the cancer patients, to determine whether two genes that ordinarily help to protect against cancer were chemically altered. They found that in sputum

from patients with squamous cell carcinoma, the promoter regions of two genes, *p16* and *MGMT*, were methylated. Methylation, the addition of a specific chemical group, can occur through exposure to cigarette smoke. Moreover, methylation inactivates these genes, making cancer more likely to develop. The methylation of these genes was detected not only after diagnosis of squamous cell carcinoma, but also in all the sputum samples that had been collected from 5 months to nearly 3 years *before* lung cancer could be clinically detected. Thus, methylation of these genes is a molecular marker that can be used to predict the development of lung cancer, the leading cause of cancer death in the United States, at a very early stage. Since people continue to smoke despite intensive efforts at controlling smoking, research that may lead to improved diagnosis and treatments at an early stage of the disease, is highly valuable.

*Therapies.* The Working Group highlighted the development of targeted therapy for chronic myelogenous leukemia (CML), a cancer that causes the development of abnormal white blood cells called granulocytes. The abnormal granulocytes are incapable of protecting the body from infection. For some time it has been known that nearly all patients with CML carry a distinctive chromosome called the Philadelphia (Ph) chromosome, which causes the production of an enzyme known as tyrosine kinase. Thus, NIH-funded scientists have carried out research leading to development of a drug to inhibit tyrosine kinase activity, and they have conducted experiments to determine whether it might be effective against CML. In studies of cell cultures and experimental animals, they found that the drug, designated STI571, stops the growth of abnormal granulocytes or causes them to self-destruct. Moreover, all human CML patients treated with STI571 had a remission of their disease, and in several patients the Ph chromosome completely disappeared. This demonstrates that laboratory research can be translated into the development of a powerful new therapeutic agent for the treatment of cancer. In addition, the Working Group noted that this development of a targeted cancer treatment is a significant advance over the traditional “shotgun” approach.

The Working Group also commented on an advance that could lead to treatments to ameliorate the toxic effects of chemotherapy on white blood cells. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is an important cytokine in the development of a specific population of white blood cells, the myeloid cells, and is used therapeutically in chemotherapy patients with low levels of these cells. Researchers discovered a novel mechanism by which production and secretion of GM-CSF is regulated. They found that a protein (tristetraprolin or TTP) causes instability of the mRNA encoding GM-CSF. This provides a new drug target for these disorders, in that inhibitors of this protein’s action might help to increase the secretion of GM-CSF, and thus increase the formation of white blood cells.

Finally, the Working Group noted that a study of the willingness of participants in clinical trials to be randomly assigned to different treatment groups provided valuable insights for clinical researchers. The study examined the willingness of women who are genetically predisposed to breast or ovarian cancer to participate in randomized clinical trials, the “gold standard” for evaluating the efficacy of a treatment or intervention. The women were asked whether they were willing to participate in a randomized trial of various interventions to reduce cancer risk, including prophylactic surgery (either a mastectomy or a hysterectomy). Only 17-19 percent of the women were willing to participate in a randomized trial, whereas most were willing to participate in non-randomized trials. The women who were willing to participate in a

randomized trial were also more willing to undergo prophylactic mastectomy and were more likely to have children. Thus, investigators are likely to have difficulty in recruiting women to participate in randomized clinical trials for breast and ovarian cancer risk reduction. The Working Group commented that this finding will likely lead to the development of new approaches to conducting such trials.

### Reproductive and Developmental Biology and Aging

The Working Group highlighted a very diverse series of advances in the areas of reproductive and developmental biology, and aging. These advances included studies of basic biological phenomena occurring shortly after fertilization, research on the biological and behavioral development of babies and children, and studies of the biological bases of aging. Thus, the research in this area spanned the entire human lifespan. One theme that came up repeatedly was the interaction of environmental and genetic influences during development—the biological outcome reflects contributions from both. This theme reoccurs in other discussion areas, such as neuroscience.

*Development of the Embryo and Fetus.* The Working Group highlighted two advances that examine biological processes relevant to the very earliest stages of embryonic development. In one, researchers found a gene in female mice, *Mater*, that is required for early mouse embryos to continue developing beyond the point at which the mouse zygote splits into two cells. The finding has implications for infertility treatment in women. In another study, scientists considered the establishment of the connection between the embryo/placental complex and the maternal blood supply, a process known as implantation. How the embryo is protected from being rejected by the maternal immune system remains a critical question. NIH-funded researchers studying this question in the rhesus monkey found that a major histocompatibility molecule known as Mamu-AG is produced at the critical stage of implantation. The scientists believe that it prevents the maternal immune cells from recognizing the embryo as foreign and rejecting it. These findings suggest that inadequate expression of the human equivalent of Mamu-AG might substantially impair the invasiveness, survival, and function of the embryo/placental complex.

*Development from Birth Through Adolescence.* The Working Group also noted the implications of a study on an animal model that shows that pain and tissue injury in newborns may enhance their sensitivity to pain later in life. This is particularly relevant to the 400,000 babies born each year in the U.S. at low birthweight or prematurely. The medical procedures used to keep them alive and monitor their progress, including heel sticks to draw blood, the insertion of IV lines, and the use of ventilators, may cause pain and tissue injury. Using rats, NIH-funded scientists showed that at a critical stage in the rat's development, equivalent to 24 weeks gestation in humans, irritation of the rat's paw caused an increase in the density of spinal cord nerve fibers in an area that propels signals to the brain. In addition, these animals reacted more strongly to pain as adults. Similar irritation when the rats were equivalent in age to adolescent humans did not change the density of nerve fibers. The study indicates that it is essential to develop approaches to limit painful stimuli to newborns.

Another study highlighted by the Working Group considered the biological causes of Sudden Infant Death Syndrome (SIDS), which in the United States is the leading cause of death of infants between one month and one year of age. NIH-supported researchers discovered that many of the infants who died of SIDS had a diminished binding of serotonin, a neurochemical that nerve cells use to communicate, in a major network of nerve cells in the brainstem. This network is believed to control respiration, blood pressure, temperature, and arousal during sleep. Thus, the deficit in serotonin binding in this network could explain why infants who sleep on their stomachs, on soft bedding, or whose faces are covered by bedding do not wake up, take a breath, and move around if they become overheated or receive insufficient oxygen. The finding may lead to the development of tests to screen for the deficiency in serotonin binding, as well as better ways of managing these babies to protect them from an untimely death.

The Working Group also noted an important advance in the role of dietary supplements in infant development. In this study, researchers established a link between formula additives and children's intelligence. Human breast milk contains the essential fatty acids docosahexaenoic acid (DHA) and arachidonic acid (AA), which are believed to play a role in the development of the nervous system. While DHA and AA are routinely added to infant formula throughout Europe and Asia, these substances are not added to infant formulas in the U.S. Some studies have shown that breast-fed babies, regardless of socioeconomic status and the mother's education, perform better on cognitive tests than formula-fed babies, while other studies have been inconclusive or contradicted these results. To determine whether DHA and AA affect mental development, researchers compared the performance on various tests of infants who received formula supplemented with DHA, both DHA and AA, or no supplementation. The researchers found that infants in the DHA/AA-supplemented groups performed significantly better on various tests of intelligence and mental development. Whether DHA and AA should be added to infant formula in this country remains a public health concern. The findings from this study serve as an important step in the comprehensive array of studies needed to determine whether DHA and AA should be added to infant formula.

Another study along the developmental continuum demonstrated the effects of intensive reading instruction on brain function and reading behavior in children. This is important because dyslexia, or the inability to read or understand what is being read, is estimated to affect 10 to 20 percent of children in the United States. Previous research has demonstrated that dyslexia usually can be prevented if the disorder is identified by first grade and followed by intensive early reading intervention. However, correcting specific reading disabilities has been extremely difficult after children reach nine years of age. Scientists attribute this lack of response to an inability of the brain to respond and adapt to language and reading instruction after this age, and to a decrease in motivation to learn to read. Working with children between 10 and 13 years of age with severe reading disability and family histories of multigenerational dyslexia, researchers reported that after these children participated in an intensive 30-hour reading and science workshop, they scored at or above grade level in reading skills. These discoveries indicate that reading disability in older children, previously thought to be unresponsive to treatment, *can* be corrected.

Finally, the Working Group commented on a rare, large-scale, longitudinal brain-imaging study using high power magnetic resonance imaging equipment. This study is unusual because it

examined the same individuals over a period of years; most studies involve comparisons of individuals of different ages. The study showed different rates of increase in the volume of the white matter and gray matter, areas of the brain involved in “signal transfer” and “thinking,” respectively. The researchers found that these regions grew at different rates, depending on age and gender. Thus, the findings imply that the maturation of certain regions of the brain is influenced by sex hormones, with females reaching brain maturity about a year earlier than males, and that the adolescent years are critical for this maturation. The availability of precise longitudinal data on brain development will be valuable in the diagnosis of disease or developmental disorders.

*Aging.* The Working Group noted several exciting studies in which genetic techniques contributed to the understanding of the biological pathways leading to aging. For example, one such study examined the molecular mechanisms underlying the increase in lifespan caused by caloric restriction. Caloric restriction—a substantially limited diet, particularly one with reduced sugar availability—has been shown to significantly extend lifespan in a wide variety of organisms. NIH-supported scientists found that they could mimic the effects of caloric restriction by mutating several genes involved in glucose metabolism, effectively lowering the cellular glucose concentration. Accordingly, this study provides a foundation for examining the fundamental pathways that may underlie aging. The Working Group also highlighted several studies that relied on microarray technology to examine the changes in the patterns of gene expression that accompany aging. Aging changes the activity of a large number of genes, but it is not known whether some of those changes cause aging, while others are effects of aging. Using microarray analysis, these studies showed that certain age-related changes in gene expression were attenuated by caloric restriction. In addition, the studies showed that some changes in gene expression accompanying aging are similar to responses to different types of cellular damage. Caloric restriction appears to increase the expression of genes involved in repairing and preventing cellular damage. Thus, microarray technology may provide an efficient approach to answering important questions about the genetic and molecular mechanisms of aging.

The Working Group also commented on the surprising insights into the cell biology of aging from studies of cloned animals. These studies examined the effect of cloning on the length of telomeres, structures at the tips of chromosomes that shorten as an organism ages. As telomeres shorten, cell division slows and eventually stops, at which point the cell is referred to as senescent. Cloning involves the development of new animals from cells from the body (somatic) cells of adult animals. Since the cells from which the animals are cloned are from adults, their telomeres are shorter than those of a fertilized egg. However, work in the last year has demonstrated that when animals are cloned, the telomere length is “reset,” suggesting that, in contrast to what might have been anticipated, these cloned animals do not have shorter lifespans. Indeed, some cloned animals may ultimately prove to have longer lifespans, consistent with the increase in telomere length produced in some cases. Thus, cloning studies may be useful for learning how telomere length is regulated, as well as its effect on aging.

The Working Group also commented on recent studies that show that older Americans have fewer disabilities, even though they are living longer. At one time, it was thought that medical advances would save people from dying, but produce old age plagued with disability and the

burden of health care services and costs. However, recent studies have shown that this prediction is incorrect. Research has begun to focus on plausible models to explain the declines in disability and to identify specific interventions or behavioral changes that could accelerate the trend toward decreased disability and improved quality of life. In addition, new paradigms in biotechnology offer promise for future acceleration of the decline in disability.

Finally, the Working Group was particularly pleased with a study of a simple, cost-effective treatment for urinary incontinence, which in the United States costs more than \$16 billion per year in direct treatment costs. The study showed that in most women, clinicians can treat the condition by providing information on pelvic anatomy along with exercises to strengthen the muscles in the pelvic floor. Health-care providers can readily incorporate these simple strategies to develop bladder capacity and control into everyday practice with women.

### Infectious Diseases and Immunology

In its discussion of NIH's contributions in the area of infectious diseases and immunology, the Working Group focused on the three broad categories of pathogens: viruses, bacteria, and eukaryotic organisms (cellular organisms containing a membrane-bound nucleus). The Group noted that the research in this area benefited from the availability of complete DNA sequence information on a number of pathogenic organisms, which were the first to be sequenced as a result of the small size of their genomes. In addition, the Group noted that many of the studies addressed an urgent public health problem—the development of strains resistant to antibiotics and other therapeutic drugs. The availability of genomic information will be invaluable in developing new drugs and vaccines to combat infectious diseases. Finally, the Group commented on the global nature of the health threat from infectious diseases. Because many infectious diseases exist only outside the United States, or the incidence of such diseases is much higher in other countries, NIH's contributions in this area are truly of global proportion.

*Viruses.* Acquired Immune Deficiency Syndrome (AIDS) is caused by the destruction of the immune system by the Human Immunodeficiency Virus (HIV). The Working Group highlighted advances in four areas that contributed to the understanding of AIDS: how HIV initially infects cells; how it evades the defenses of the body's immune system; how it re-emerges after antiretroviral treatment; and the contribution of primate animal models to the overall understanding of AIDS. The first study highlighted by the Group identified a protein that may play a critical role in HIV pathogenesis by transporting the virus from the mucosal and dermis layers in the rectum, vagina, and cervix to remote lymph nodes, where it infects its primary target, the T cells of the immune system. In another study, NIH-funded scientists used mass spectrometry to characterize the 3-dimensional shape of a portion of an HIV envelope protein that is recognized by antibodies produced by infected patients. The study has important implications for the understanding of the immune response against HIV, and could contribute to the development of a vaccine. The Group also highlighted a study that examined the re-emergence of infection following the discontinuation of highly active anti-retroviral therapy. Although it had been hoped that such therapy could completely clear the virus in infected individuals, previous studies had shown that HIV from latently infected CD4+ T cells rapidly reemerges following discontinuation of therapy. The new study demonstrated that infected individuals who received antiretroviral therapy have other sources of resurgent virus, in addition

to the CD4+ T cells. In sum, these NIH-supported studies have substantial implications with regard to the prevention and treatment of HIV.

The Group also discussed the invaluable role of primate animal colonies and studies of the simian immunodeficiency virus (SIV) in understanding AIDS. NIH had funded the primate colonies for many years before the advent of AIDS. Unexpectedly, dozens of animals became dangerously thin and weak, developed tumors, anemia, and severe infections. Researchers found that the animals were infected with a then-unknown infectious organism, a retrovirus. Eventually, this led to the discovery of SIV, which produces an AIDS-like syndrome in primates. SIV infection of macaque monkeys is now widely considered the best animal model for human AIDS. It is used by hundreds of researchers worldwide to study many features of the disease, including its transmission, the immune response to the virus, and the nature of the brain and nerve damage it produces. It has also been extremely useful for the evaluation of experimental vaccines and therapeutics. These studies are testimony both to the value of animal models and the critical role of serendipity in the research process.

The Working Group acknowledged the importance of the studies conducted by the NIH-supported researchers who studied the Ebola virus, an extraordinarily virulent pathogen that kills up to 90 percent of infected individuals, sometimes devastating entire African villages. Due to its virulence, the virus is very difficult and risky to study. Nonetheless, NIH-funded researchers identified the Ebola gene and gene product, which enables the virus to attach to cells that line the interior of blood vessel walls, called endothelial cells. The gene product, a glycoprotein (a protein-carbohydrate conjugate), also facilitates the insertion of viral genetic material into the endothelial cells. Thereafter, the rapid production of the glycoprotein destroys the endothelial cells, causing the blood vessel walls to become thinner and eventually to bleed. When the scientists altered the gene so as to prevent the protein from binding a carbohydrate, they found that the endothelial cells remained intact. Thus, production of this glycoprotein leads to the destruction of the endothelial cells, and ultimately, massive hemorrhaging and death. The characterization of the cellular process leading to the massive hemorrhaging characteristic of Ebola fever may eventually lead to the development of a vaccine, and effective treatment measures.

Research on hepatitis C was also highlighted by the Working Group. Approximately 80% of persons infected with the hepatitis C virus (HCV) become persistent carriers of the virus and generally have associated evidence of chronic hepatitis. In approximately 20%, the chronic hepatitis may progress to cirrhosis and liver-related fatality. The reason why most individuals fail to clear the virus is unknown and there has been no way to predict who will recover from HCV infection and who will develop persistent infection. Using stored samples previously obtained in prospective studies of transfusion-associated hepatitis C, scientists extracted and amplified viral nucleic acid (i.e., “genetic material”) at various time points early in HCV infection and then measured changes (mutations) in the nucleic acid structure of the viral envelope. It has been known that HCV exists as a population of closely related but immunologically distinct variants that have been termed the quasispecies. In patients who recovered from HCV infection, the degree of viral diversity decreased as the patient developed antibodies to HCV. By contrast, patients who developed chronic infections showed a dramatic increase in viral diversity. The decrease in diversity in patients who recovered indicated that the immune response was able to



contain viral replication, leading to clearance of the virus from their bodies. Thus, as noted by the Working Group, the existence of distinct quasispecies of HCV, some of which are resistant to the immunological response of an infected person, explains why some individuals recover from HCV while others develop persistent infection. Moreover, the research implies that HCV infection can be fought not only with anti-viral drugs, but also with therapeutic approaches that would broaden and intensify the immune response.

*Bacteria.* The Working Group lauded a number of NIH-supported studies that illustrate the power of genetic techniques to unravel the basic mechanisms underlying bacterial infection, virulence, and persistence in human hosts. In one series of studies, NIH-supported researchers analyzed the genetic make up of more than 500 strains of *Helicobacter pylori*, a bacterium that is a major cause of peptic ulcer disease and risk factor for gastric cancer. The study, which was designed to gain insight into the evolution of this pathogen and identify factors that affect its ability to produce disease in people of particular ethnicity, identified three major strains of the bacterium with different geographic and ethnic distributions. Two other studies focused on *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis, a disease which is characterized by dormant or “persistent” infection in most affected individuals. NIH-funded scientists used genetic techniques to show that two bacterial genes underlie the ability of *Mycobacterium* to persist in clusters of human “scavenger” cells that engulf them and attempt to digest them. The other study identified and functionally characterized a gene that facilitates the formation of rope-like strands of *Mycobacterium*. The formation of such strands is correlated with the virulence and persistence of the bacterium. After developing a more efficient “knockout” technique for use in *Mycobacterium*, the scientists showed that when they inactivated the gene that facilitates the formation of rope-like strands, the bacteria were much less infectious, and less capable of causing persistent disease and death in laboratory mice. These studies contribute to the understanding of bacterial infection and disease, and may lead to new strategies for disease prevention and treatment.

The Working Group was enthusiastic about a study in which researchers created a synthetic antibiotic molecule out of non-natural forms of amino acids called beta-amino acids. This “beta-peptide” mimics a class of natural antimicrobial molecules called magainins. These molecules exist in a wide variety of forms in nature and defend biological borders, such as skin, from invading bacteria. The beta-peptide exhibits its antibiotic properties in the laboratory, killing both normal and drug-resistant strains of infectious bacteria, including a strain resistant to vancomycin – the “last resort” antibiotic that must be administered intravenously in a hospital. Because drug-resistant bacteria are now a global health threat, a new type of antibiotic to which bacteria may not become resistant would be very valuable.

*Eukaryotes.* The Working Group highlighted a number of studies that examined the transmission of malaria by mosquitoes, how the body resists malarial infection, and the efficacy of drugs used to combat the disease. These studies are particularly important because about 110 million people develop the disease annually, of which about 1 million die. Malaria is caused by the parasite *Plasmodium*, which is transmitted to humans by the *Anopheles* mosquito. Because *Anopheles* is not easily grown in the laboratory, the details of how *Plasmodium* survives in the mosquito’s digestive tract and salivary glands before it is transmitted into the blood of another person are not known. To avoid the difficulty of working with *Anopheles*, NIH-supported scientists learned

how to grow *Plasmodium* in the fruit fly, *Drosophila melanogaster*. Because *Drosophila* is closely related to the mosquito and its genome has been fully sequenced, it is an excellent model to identify the genes that control the insect's immune response to the parasite. Using *Drosophila*, scientists determined that macrophages, "scavenger" cells that engulf and destroy microorganisms, play a key role in the fly's response to *Plasmodium*. The use of *Drosophila* as a model should greatly accelerate efforts to understand the key steps in malaria transmission.

Another study highlighted by the Group showed that a new red blood cell mutation (a null mutation of the FY antigen) is associated with resistance to malaria in Papua, New Guinea. The mechanisms by which these mutations modulate malaria are not known. Most Africans lack the Duffy blood group antigen FY and appear to be protected from *Plasmodium vivax* infection, a more "benign" form of malaria, which is relatively uncommon in Africa compared to other malaria endemic areas of the world. For example, *P. vivax* is holoendemic with other forms of malaria in Papua, New Guinea, where many mutations in hemoglobin and red cells are known to exist. These data suggest that *P. vivax* infection is involved in the selection of red blood cell genetic variance and that the new mutation may diminish the protective effect of alpha thalassemia mutation. Further understanding of natural selection for mutations that affect the frequency and severity of malaria will help to develop novel strategies to combat this disease.

Finally, the Working Group highlighted two advances dealing with the efficacy of drugs used in the treatment of malaria. The first elucidated the development of resistance to chloroquine treatment by *Plasmodium falciparum*. For decades, chloroquine has been the drug of choice for the treatment of malaria because of its efficacy, lack of toxicity, and affordability, but many strains of *P. falciparum* are now resistant to it. NIH-supported scientists showed that a mutation in the *pfcr* gene of *P. falciparum* is responsible for the development of chloroquine-resistance. Identification of the function of the gene product will enable scientists to better understand the molecular mechanisms of drug resistance, and develop new antimalarial drugs to combat this devastating disease. The other study showed that red blood cells infected with the malaria parasite develop tiny channels that permit the passage of certain ions, organic solutes, and nutrients necessary for growth of the parasite. Because these channels form only in infected red blood cells, scientists could develop new anti-malarial drugs that block the channels and cut off the parasite's nutrient supply, without affecting uninfected blood cells. Such drugs could supplement or supplant the use of chloroquine, particularly when the disease is due to a chloroquine-resistant strain.

### Neuroscience and Behavior

Neuroscience is an incredibly diverse area of interdisciplinary research, covering molecules to behavior, and not just behaviors of individuals, but behavior of organized societies. Many of the advances in the past year have been at the molecular and cellular level. Nonetheless, the nervous system primarily exists to compute behavior, and the research highlighted by the Working Group encompassed that aspect of neuroscience, as well as various advances in the understanding of sensory systems, plasticity of the nervous system, neurological diseases, and injury.

*Sensory Systems.* The Working Group was enthusiastic about a number of NIH-funded studies relating to the molecular mechanisms underlying normal hearing and hearing loss. In one study,

scientists identified the gene that codes for a protein critical to the function of the cochlear outer hair cells, which are cells in the inner ear responsible for our ability to discriminate different tones. The protein, called *Prestin*, is expressed only in the outer hair cells, and is essential for rapid changes in the length of the outer hair cells that accompany the detection of sound. The study raises the question whether naturally occurring mutations of *Prestin* and other genes uniquely associated with hearing are responsible for certain types of hearing impairments in humans. The Working Group noted that this question has been under active investigation by scientists who, during the last few years, have mapped and cloned the genes responsible for a large number of common hearing disorders. Characterization of the gene products involved in these disorders, such as was done with *Prestin*, will provide critical information about the basic molecular mechanisms of hearing. In addition, this highly successful effort in determining the genetic bases of hereditary hearing impairments has fundamental implications for treating individuals with these disorders.

The Working Group also lauded a variety of advances in vision research. These advances ranged from research on a photoreceptor protein, rhodopsin, which mediates the first step in the initiation of vision by light, to studies on the brain circuitry responsible for visual perception. NIH-supported scientists contributed to the understanding of rhodopsin by determining its structure at the atomic level. The work is particularly important because this detailed knowledge of rhodopsin's structure will help scientists understand how it initiates the next step in the visual process, the activation of a protein involved not only in vision, but also in the detection of other stimuli such as hormones, ions, and odorants. Other studies used genetic methods to study the regulation of gene expression of a different protein critical to the initial steps in the detection of light. The medical implications of these studies are substantial, because it is known that mutations in this gene cause retinal degeneration and blindness. Indeed, in a dramatic advance, scientists showed that "knockout" mice that do not have this gene exhibit a retinal degeneration similar to that in humans, but that vision can be restored by feeding the mice a form of vitamin A that is not normally present in the diet. Thus, basic research such as this not only improves our understanding of the molecular mechanisms of the visual process, but also may lead to treatments for retinal degenerations.

The Group also noted the value of another study relevant to age-related macular (central retinal) degeneration, the leading cause of blindness in patients over 65 years of age. Currently, these patients are treated with laser photocoagulation, but some patients do not improve or even continue to lose their vision. The NIH-supported study was based on previous studies that have shown that patients who have age-related macular degeneration have unusually high levels of vascular endothelial growth factor (VEGF). To study the hypothesis that high levels of VEGF cause the degeneration, NIH-supported scientists developed a model of the disease in rodents by using gene transfer to increase the production of VEGF. The researchers found that the rats developed abnormal blood vessels similar to those in humans with macular degeneration, as well as those in other related diseases such as diabetic retinopathy. Studies such as this one may lead to new ways to prevent the development of disease, rather than treat it after vision has already been affected.

The Working Group commented on the exciting possibilities raised by the discovery in rodents of a naturally occurring brain chemical, anandamide, which reduces the perception of pain.

Because anandamide is chemically unrelated to the major class of pain-reducing drugs, the opiates, it raises the prospect of a nonaddictive treatment for pain that avoids the undesirable aspects of opiate analgesics such as morphine.

*Plasticity of the Nervous System.* The Working Group noted the merit of an animal model study of the role of sensory input in determining the characteristics of the brain. In that study, scientists showed that following “rewiring” of the ferret brain by surgically routing nerves from the eye to a part of the brain that usually receives input from the ear (auditory cortex), the rewired brain acquires characteristics of the brain typical of the visual cortex, which ordinarily receives input from the eye. Specifically, the rewired auditory cortex exhibited columns of cells representing the orientations of visual stimuli. Moreover, behavioral studies showed that these animals can “see” with the part of their brain that ordinarily receives auditory input. This study shows that the development and organization of the brain depends on the nature of the input, i.e., the brain exhibits “plasticity.”

In addition, the Working Group highlighted research that used the fruit fly, *Drosophila*, to study a gene involved in learning. Although one might not immediately think that learning could be productively studied in the lowly fruit fly, it is particularly valuable for studies of this type because its brain is simpler than the mammalian brain, and transgenic animals with specific genetic characteristics can be produced with through genetic engineering. The NIH-supported researchers found that a novel gene given the name “latheo” is involved in learning in *Drosophila* by regulating the formation of synapses, connections that relay signals between neurons. Thus, this study contributes to the understanding of synaptic plasticity underlying long-term memory and learning. Moreover, it provides basic genetic and molecular information that is relevant to the understanding of mammalian and human learning and learning disorders.

Another advance highlighted by the Working Group illustrated how basic research on the role of synaptic plasticity in memory and learning may have unexpected, practical implications. In that study, NIH-funded scientists found that the addictive properties of nicotine are due to changes in synaptic strength similar to those that occur during learning and memory formation. Specifically, the scientists found that nicotine acts on nerve terminals in a certain part of the rat brain to enhance the release of a neurotransmitter called glutamate. This, in turn causes increased release of the transmitter dopamine from the “reward” centers of the brain, which play a critical role in addictive behaviors. Furthermore, by showing that nicotine causes enhancement of synaptic transmission by acting on a particular type of receptor, the study reveals a possible target for medications that could help smokers quit.

*Neurological Disease and Injury.* The Working Group lauded an NIH-supported study in which scientists developed a new animal model of human Parkinson’s disease using fruit flies that were genetically engineered to produce many of the essential features of the disease. The scientists created transgenic *Drosophila* that produce an aberrant form of a protein,  $\alpha$ -synuclein, implicated in the development of familial Parkinson’s disease. These flies exhibit many essential features of human Parkinson’s disease, including age-dependent onset, chronic progressive loss of dopamine neurons and motor function, and development of the fibrous deposits characteristic of Parkinson’s brains. The fly model will be useful for understanding the role of the aberrant protein in the development of Parkinson’s disease, and may also be invaluable in screening

potential drugs to treat, or even prevent, Parkinson's disease. Similarly, the Working Group highlighted an important advance in the biology of Alzheimer's disease. In that study, scientists identified an enzyme that cleaves a large protein into smaller peptide fragments called amyloid- $\beta$ . These amyloid- $\beta$  fragments build up in the brains of patients with Alzheimer's disease, and are implicated in the loss of memory and cognition that are the hallmarks of the disease. The finding is significant because it suggests that scientists could develop a drug to act on the enzyme and inhibit the production of amyloid- $\beta$ , thus preventing or delaying the development of Alzheimer's disease.

The Working Group was highly enthusiastic about a study that suggested a possible source of new neurons, or "nerve cells," that can be used to replace those that have been lost due to brain or spinal cord injury or disease. Because new neurons are not generally produced by the adult brain and spinal cord, a source of such cells is critical. Surprisingly, NIH grantees found that rodent and human bone marrow stromal cells, which ordinarily develop into bone, cartilage, and fat cells, could be stimulated with certain chemicals to develop into neurons—thus yielding extremely interesting information about the potential plasticity of cells that have already developed into a particular functional type. If the neurons produced in this way can be stimulated to become integrated into the nervous system, the bone marrow stromal cells could offer a readily accessible, easily renewable source of replacement neurons without the risk of obtaining them from the brain. Moreover, because these cells could be obtained from a patient's own body, they would avoid problems of immunological incompatibility, as well as ethical concerns that might arise from other sources of replacement cells.

*Behavior, Emotion, and Learning.* The Working Group applauded an NIH-supported behavioral study that represents a paradigmatic change in the characterization of the human response to stress. This response, which is based on studies of males, has been viewed as a "fight-or-flight" response. The stress response in females was less well understood, because of their cyclical hormonal variation. NIH-supported studies found that rather than "fight-or-flight," females engage in a response to stress that could be characterized as "tend-and-befriend." This pattern stems from females' protection of offspring under stressful circumstances, and their participation in social groups for protection and the exchange of resources. The researchers believe that these responses depend in part on female hormones such as oxytocin and estrogen, as well as other physiological mechanisms. This interesting new model is a rare example of evolutionary biology's influence on NIH-supported research. It opens a fresh field of inquiry in stress research, particularly in regard to the role of hormones in establishing social bonds.

The Working Group also cited another series of NIH-supported studies on the mechanisms of behavior. These studies probed the brain circuitry responsible for the influence of emotions on decision-making. The studies showed that damage to certain parts of the brain system underlying emotions, such as the amygdala, the cingulate cortex, the insular and ventromedial prefrontal cortex, may make it impossible for previously well-adapted individuals to observe social conventions, or to decide advantageously on matters pertaining to their own lives, despite well preserved learning, memory, language, attention, and other intellectual functions. These findings have direct implications for understanding several psychopathologies including depression, schizophrenia, pathological gambling, attention deficit, and hyperactivity disorder (ADHD), as well as for understanding many serious consequences of brain injury in children and

adults. This line of work is also providing insights into the biological mechanisms of normal cognition and emotion.

In the area of addiction research, the Working Group noted a study that using “knockout” mice to identify a gene involved in the reinforcing aspects of alcohol—the biologically driven desire to drink. In this study, NIH-supported scientists “knocked out” the gene that codes for the mu opioid receptor—a naturally occurring brain receptor thought to underlie the sedative effect of alcohol that makes people want to drink, even to the point of alcoholism. When these mice lacking the mu opioid receptor gene were placed in a situation in which they could easily self-administer alcohol, they did not drink it, whereas genetically normal mice did. This work suggests that the mu opioid receptor has a significant role in the propensity to drink, and illustrates the power of gene knockout techniques for understanding the mechanisms of many biological phenomena, including complex behaviors such as alcoholism. In addition, the study will open up new avenues of research that could lead to the development of medications for the treatment of alcoholism.

### Cardiopulmonary, Renal, and Pulmonary Biology and Disease

The Working Group’s discussion of cardiovascular, renal, and pulmonary biology and disease echoed the themes in other areas. Some of the studies illustrated the power of genetic techniques in understanding conditions stemming from multifactorial traits as well as those caused by single genes. Other studies demonstrated the interaction of genetic factors and the environment during development or in the processes leading to disease. Many of these studies have substantial implications with regard to the development of preventive and therapeutic measures for particular diseases or conditions.

*Genetic Approaches to Cardiovascular, Renal, and Pulmonary Biology.* The Working Group was enthusiastic about several studies of polycystic kidney disease (PKD), which affects about 500,000 people in the United States, and is the fourth leading cause of kidney failure. A disease of genetic origin, it is characterized by massive enlargement of the kidneys associated with growth of multiple fluid-filled cysts. Scientists have discovered that mutations in the genes known as *PKD1* and *PKD2* are responsible for the development of autosomal dominant PKD (ADPKD). In addition, it is known that the PKD genes code for proteins called polycystins. In recent studies of mice with mutations in the PKD genes, NIH-supported scientists determined that one form of polycystin is essential for the normal development of the kidney, heart, and pancreas. Moreover, in another series of experiments, researchers showed that a drug that acts on an enzyme critical for growth factor signaling reduced cysts, improved kidney function, decreased liver abnormalities, and increased life span in a mouse model of the disease. When drug treatment was stopped, the disease returned. These research advances contribute to the understanding of the molecular and cellular events in PKD, and may lead to the development of safe and effective therapies for this disease. In particular, further research on growth factor signaling pathways could lead to clinical trials of possible therapies for PKD.

Other studies highlighted by the Working Group illustrate the power of genetic information to contribute to the understanding of inherited heart diseases. In these studies, NIH-supported scientists identified several genetic mutations that affect the functions of the contractile proteins

actin and  $\alpha$ -tropomyosin, thus causing hypertrophic cardiomyopathy. This condition, which involves a thickening of the heart muscle that interferes with its pumping ability, is the most common cause of sudden cardiac death in apparently healthy young individuals such as athletes. The scientists found that the clinical outcome varied depending on which mutation was involved, and the nature of the mutation's effect on the heart's contractile apparatus. This finding will be valuable in predicting the severity of the disease, in deciding among different treatment options, and in the genetic counseling of prospective parents.

The Working Group also noted the identification of the first molecular lesion, or mutation, underlying a pregnancy-induced form of hypertension, a common public health problem. This condition was attributable to mutations in a receptor that cause a normal hormone of pregnancy—progesterone—to act in an abnormal way. The mutation affects how salt is absorbed in the kidney. This new understanding of salt handling in the kidney could lead to genetic tests to identify women at high risk for pregnancy-exacerbated hypertension and the common complication, pre-eclampsia, as well as new treatments for hypertension.

Another study noted by the Working Group illustrated the possible interplay of genetic and environmental factors in cardiovascular development. The study showed that a gene underlying the body's response to certain environmental contaminants also has a role in blood vessel development. Scientists developed mice lacking the gene coding for the aryl hydrocarbon receptor, which regulates the body's responses to polycyclic aromatic hydrocarbons such as those found in cigarette smoke, the industrial chemical dioxin, and the wartime defoliant Agent Orange. They found that the vasculature of these mice remained in an immature, fetal state, adversely affecting the development of the liver, eye, and kidney. The apparent dual role of this receptor in vascular development and the response to environmental contaminants is not altogether unexpected. Although the receptor was discovered as a result of experiments examining the response to environmental toxicants, it clearly evolved for other important reasons. However, the bifunctional nature of the aryl hydrocarbon receptor suggests that scientists should look for possible effects of polycyclic aromatic hydrocarbons on the vascular system.

#### *The Role of Dietary Factors in Cardiovascular, Renal, and Pulmonary Biology and Disease.*

The Working Group stressed the value of NIH-supported studies that showed that dietary sodium intake increases the risk of cardiovascular disease among those who are overweight.

Observational studies have repeatedly identified an independent, positive relationship between dietary intake of sodium and blood pressure level. Moreover, clinical trials have demonstrated that reduced sodium intake leads to a reduction of blood pressure in patients with hypertension as well as persons with normal blood pressure. Although high blood pressure is strongly associated with risk of stroke and heart attack, the link between a high-sodium diet and these adverse events has not been clearly established. Researchers following a large, representative group of U.S. adults for 20 years found that high sodium intake is strongly associated with an increased risk of mortality, particularly cardiovascular disease mortality, in overweight persons. Among adults who were overweight, those who consumed the highest amounts of sodium were 63 percent more likely to die of cardiovascular disease than those who consumed the lowest amounts of sodium. No significant association between dietary sodium intake and risk of cardiovascular disease was found in normal-weight persons. These findings suggest that recommendations to

prevent cardiovascular disease should emphasize both weight loss and sodium reduction and that, among persons who have difficulty losing weight, greater attention to reductions in salt intake may be warranted.

*Studies with Direct Therapeutic Implications.* Sickle cell anemia is one of the most prevalent inherited diseases. Significant problems in a number of organs, including the lungs, can occur when there is sickling of the red blood cells as a result of low levels of oxygen in the blood, dehydration, or infection. The sickled cells can alter flow in blood vessels, and, in rare instances leads to premature death. This severe sickling with organ damage produces sickle cell “crisis.” Nitric oxide is a naturally occurring gas in the body that dilates blood vessels, thereby increasing blood flow. Inhaled nitric oxide binds to hemoglobin and is released as the blood circulates through the body. The resulting vasodilation and increase in blood flow may benefit patients with sickle cell anemia who have impaired blood flow in small blood vessels. Therefore, inhaled nitric holds promise as a new treatment for sickle cell anemia.

Finally, the Working Group highlighted a study of the biological mechanisms underlying the formation of abdominal aortic aneurysms, in which a weak area of the aorta balloons out, sometimes rupturing and causing death. Scientists showed that an enzyme called matrix metalloproteinase-9 (MMP-9) is responsible for the development of the aneurysm following aortic wall injury in mice. Moreover, the researchers showed that treatment with the antibiotic doxycycline, which is known to impede MMP-9 production, reduces the formation of aortic aneurysms. The value of doxycycline was also illustrated in humans; MMP-9 production in artery walls was much lower in patients who had taken doxycycline before surgery to remove aneurysm tissue. This research suggests that treatment with doxycycline has the potential to prevent small aneurysms from developing into large ones, thereby diminishing the need for expensive, risky surgery.

#### Endocrinology, Metabolism, Musculoskeletal and Skin Diseases, and Dermatology

The Working Group highlighted the many significant advances made in this area during the last year, particularly in the endocrinology of diabetes and musculoskeletal biology. Many of these studies not only elucidated the basic molecular and cellular physiology of these systems, but also suggested potential molecular targets for new drugs to prevent or treat diseases or disorders. For example, the research suggested possible drug targets for the prevention of the cardiovascular damage that occurs in diabetes, and others to stimulate bone formation and inhibit its loss. The Working Group commented that the identification of such targets would probably be the major means for drug discovery and development in the 21<sup>st</sup> century.

*Biological Mechanisms Underlying the Development of Diabetes and Its Complications.* The Working Group highlighted several studies that examined the biological mechanisms underlying the development of type 1 and type 2 diabetes. It is known that the immune system of people with type 1 diabetes attacks the insulin-producing cells of the pancreas as if they were foreign, harmful agents such as bacteria or viruses. Thus, in individuals with type 1 diabetes, the immune system produces cells and autoantibodies that lead to the destruction of the insulin-producing cells, necessitating insulin injections to enable the body to utilize glucose. In one study, NIH-funded scientists found that infants who had insulin autoantibodies in blood samples taken from



them at nine months of age developed type 1 diabetes by their fourth birthdays. Another study examined the molecular mechanisms underlying the aberrant destruction of the insulin-producing cells by the immune system. In that study, scientists found that mice susceptible to diabetes had a small change in the major histocompatibility complex (MHC), a group of proteins present on the surface of immune cells that helps separate self from potentially harmful, foreign antigens. While the change was small, its effect was to enlarge the range of antigens that interact with the MHC, suggesting that it could be responsible for the aberrant destruction of insulin-producing cells. Moreover, some people with type 1 diabetes exhibit a similar change in the MHC. Collectively, these studies may enable identification of individuals at risk for developing type 1 diabetes, and permit intervention prior to irreversible damage to the insulin-producing cells in the pancreas.

NIH-supported researchers also examined the molecular mechanisms underlying the development of type 2 diabetes, which is characterized by insufficient insulin production, and resistance to insulin action. One study provided evidence for a link between a pathway of glucose metabolism and programmed cell death, or “glucose-induced apoptosis.” In animal studies, researchers found that the addition of glucose molecules to certain proteins (glycosylation) in the insulin-producing beta cells of the pancreas may lead to apoptosis. In genetically susceptible individuals, excessive glucose-induced apoptosis may decrease insulin production to the point where type 2 diabetes develops. This is the first demonstration of a possible mechanism underlying the effect of severe or prolonged hyperglycemia in producing beta cell death and subsequent type 2 diabetes. Most importantly, this research has identified a potential molecular target for rational drug development to prevent type 2 diabetes. Other studies used genetic techniques in mice to examine the roles of the insulin receptor and two other proteins that mediate insulin action in regulating the responses of different tissues to changes in blood glucose levels. These studies led to a better understanding of insulin resistance by showing that more than one protein is involved in the responsiveness of a given tissue to changes in glucose levels, and that beta cells that are insulin resistant have an impaired ability to produce and secrete insulin. In addition, these studies suggest that type 2 diabetes is a polygenic inherited disease.

The Working Group noted the importance of NIH-supported studies that help explain how elevated blood glucose leads to long-term cardiovascular complications. Recently, it has become clear that hyperglycemia may damage endothelial cells, which line blood vessels, leading to micro- and macrovascular abnormalities. This damage can be caused, in part, by a chemical reaction between glucose and proteins on the endothelial cell surface. A fuller understanding of the glucose-protein interaction and cellular responses might permit development of therapies to limit injury to the blood vessel and surrounding tissue. Scientists found that a protein called CD59 – bound on the surface of endothelial cells – is a target for modification by glucose. Identification of CD59 as a target for modification by glucose represents an important step forward in understanding of diabetes complications. Modified CD59 can be detected in patients, and agents that block this reaction may inhibit the development of vascular disease. Interestingly, the region of CD59 modified by glucose is present only in the human form of the protein, offering a possible molecular explanation for some of the uniquely human aspects of the disease and possibly explaining why this disease has proven so difficult to replicate completely in animal models. In another study, researchers characterized a different biochemical pathway

leading to glucose-mediated damage. That pathway involves the production of a damaging form of oxygen, known as superoxide. Normalizing the level of superoxide blocked several different biochemical pathways that can lead to damage. These studies could lead to the development of therapies to limit diabetes-induced injuries to blood vessels.

*Control of Bone Loss and Formation.* The Working Group highlighted a study of the control of bone mass by a hormone called leptin, which controls body weight and gonadal function. NIH-supported investigators studied the effect of leptin on bone formation in genetically obese strains of mice, which are deficient in leptin or its receptor. Usually, high body weight results in high bone mass. However, these mice also have defects in the development of sex organs, and high levels of a naturally occurring hormone called cortisol, which produces effects similar to steroid drugs. Hormones produced by sex organs are necessary to maintain bone mass, and steroids like cortisol usually cause bone loss. Thus, the researchers were surprised to find that the mice had very high bone mass. Furthermore, they found that the high bone mass was due to the absence of leptin function rather than the obesity. Specifically, the researchers found that leptin indirectly suppresses the bone-forming activity of osteoblasts through its action on a part of the central nervous system called the hypothalamus. This discovery revealed a previously unknown mechanism by which bone formation is regulated. If drugs can be designed to block leptin's action, they may be useful in anabolic therapies to form new bone. The Working Group commented that the need for drugs to restore and rebuild new bone is compelling, particularly because osteoporosis is one of the world's most common diseases.

The Working Group also commented on a study of a molecular mechanism of bone loss or resorption. Bone resorption by cells called osteoclasts is a normal part of bone remodeling, in which old or damaged bone is replaced with new bone. People who have insufficient bone resorption during early growth develop a disorder called osteopetrosis. Studies have suggested that special proteins called proton pumps are essential to bone resorption, because they produce the acidic environment essential for dissolution of the mineral components of bone. Thus, to examine the role of proton pumps in bone resorption, NIH-supported researchers created a genetically modified mouse in which a gene coding for a proton pump protein was inactivated. The mice exhibited the skeletal abnormalities characteristic of osteopetrosis, and osteoclasts from the mice were unable to resorb bone when tested in cell culture. The work suggests that the proton pump protein is essential to bone resorption, and that the development of drugs that block its action could provide a new approach for preventing bone loss.

*Other Advances in Endocrinology and Dermatology.* The Working Group highlighted a study that identified a new molecule essential for normal wound healing. Each year, more than four million people are afflicted with chronic non-healing wounds such as diabetic ulcers, bedsores, venous ulcers, and acute nonhealing wounds in the elderly. These impaired healing states are characterized by tissue destruction and in many cases by bacterial infection, leading to the hypothesis that SLPI (Secretory Leukocyte Protease Inhibitor), a peptide expressed during normal skin wound healing, may play a major role in this process. SLPI is a peptide with anti-inflammatory, anti-viral, anti-fungal, and anti-bacterial properties that is found in fluids that bathe mucosal surfaces, such as bronchial fluids, cervical fluids, and saliva. NIH-funded scientists showed that "knockout" mice lacking the SLPI gene have markedly impaired skin wound healing, increased inflammation, and chronic wounds. Topical application of SLPI

reversed the abnormal condition, and enhanced healing. The Working Group noted that the study could lead to the development of ways to improve wound healing in many diseases and disorders.

The Working Group also commented on a study that found that early childhood stress, resulting in elevated levels of certain hormones, may predict vulnerability to alcoholism. The scientists found that infant monkeys reared apart from their mothers displayed exaggerated reactions to moderately stressful situations as adults, and also drank more alcohol than did monkeys raised by their mothers. The deprived monkeys also exhibited high levels of corticotropin-releasing hormone, which is known to regulate the body's response to stress. These findings suggest that emotionally disruptive early-life experiences predict alcohol consumption later in life.

### Clinical Populations and Health Care Delivery

The Working Group was enthusiastic about the diversity of studies in the areas of clinical epidemiology, health care delivery, and the human response to health care. These studies addressed diseases that create enormous economic burdens as well as pain and suffering, and thus are of great concern to the public and health care professionals. By examining treatment efficacy or health outcomes in large-scale studies, NIH-supported research helps determine which best treatments and health care regimens are best. And by studying ways to improve health care delivery and improve the human response to health care, NIH facilitates the availability and use of those treatments and regimens.

*Clinical Epidemiology.* The Working Group highlighted a number of epidemiological studies that evaluated different treatments for various diseases or conditions, to determine which treatment produces the best health outcome. For example, two studies examined whether menopausal hormone replacement therapy, commonly prescribed for many women, increases a woman's chance of developing breast cancer. Because the effect of combined estrogen and progestin therapy on breast cancer risk has been controversial, NIH-funded researchers examined the association between menopausal hormone therapy and breast cancer risk in 46,000 women who had used hormone replacement therapy within the last four years. They found that combined estrogen-progestin treatment increased the risk of breast cancer more than estrogen alone, but estrogen alone also increased the risk as compared to no therapy. Short-term therapy of two to three years was not associated with an increased risk of breast cancer. In another study, researchers found that estrogen replacement therapy did not increase the risk of breast cancer among women with a history of benign breast disease. In view of the favorable effects of hormone replacement therapy on the heart, bones, and overall quality of life, these studies support its use by menopausal women, at least on a short-term basis.

The Working Group also emphasized the importance of two multicenter clinical trials that assessed the effect of improved blood glucose control on the development of eye, kidney, and nerve complications stemming from type 1 diabetes. The first trial, which lasted 10 years and involved over 1,400 people, compared conventional therapy with intensive therapy that aimed to maintain blood glucose as close to normal as possible. The study showed that control of blood glucose, as measured by the level of glycosylated hemoglobin, was much better with intensive therapy. Moreover, this intensive therapy substantially decreased the development of diabetic

eye, kidney and nerve complications. The followup of persons in this trial examined the long-term effects of intensive therapy and improved blood glucose control. Surprisingly, the researchers found that people who had received intensive therapy during the trial continued to have a lower risk of eye and kidney disease than those who had received conventional therapy, despite an increase in glycosylated hemoglobin during the follow-up period. These findings suggest that early initiation of intensive therapy, continued for as long as possible, will have a beneficial effect on the long-term eye and kidney complications resulting from type 2 as well as type 1 diabetes. Thus, the Working Group emphasized the potential for a huge impact of these studies on the enormous pain and suffering from diabetes, as well as the economic burden.

In addition, the Working Group commented on the Prostate Cancer Outcomes Study (PCOS), an ongoing evaluation of the optimal treatment for prostate cancer, which will be diagnosed in over 180,000 men in the year 2000. The study, which has supplied badly needed data, is the most comprehensive population-based outcomes study ever conducted on prostate cancer. Data collected as part of the PCOS has shown that specific treatments, such as radiation therapy, radical prostatectomy, and hormonal therapy, can have detrimental effects on urinary, bowel, and sexual functions. In addition, PCOS data showed that elevated prostate specific antigen is one of the strongest predictors of spread of the disease outside the prostate. By collecting comprehensive data on the health outcomes of various treatments for prostate cancer, the study will help men, their families, and physicians make decisions about treatment options.

*Health Care Delivery.* The Working Group pointed out the importance of a study that compared the quality of care received by fee-for-service Medicare recipients with those enrolled in HMOs. The study compared the health care outcomes of elderly patients who had suffered an acute myocardial infarction and been cared for at 20 Minnesota community hospitals. The researchers found no difference between the outcomes of patients in fee-for-service programs and those in HMOs. Indeed, HMO patients received superior care in some respects—they used emergency transportation more frequently, especially when their symptoms appeared at night; and they received aspirin therapy more often. All other indicators of quality were identical for the two groups: involvement of a cardiologist; treatment delay; time to electrocardiogram; use of thrombolytic agents; and time from hospital arrival to initiation of thrombolytic therapy. The Working Group was particularly impressed with this study because of the difficulty of conducting such research in the rapidly changing health care environment. Moreover, they noted that because health care providers have economic interests in health care delivery, NIH's role in conducting unbiased studies of this type is indispensable.

The Working Group was also impressed by a study relevant to health disparities arising from cultural differences in language. The study concluded that African Americans and Caucasians use different words to describe the breathlessness that occurs during an asthma attack. Specifically, African Americans studied in a laboratory setting used more upper airway descriptors than Caucasians. Increased sensitivity of health care professionals to these cultural language differences should improve their assessment of asthma symptoms in African Americans, and may also prevent under-treatment of acute asthma episodes.

The Working Group commented on the practical value of a study that demonstrated that opioid drug injectors are more likely to use methadone treatment when it is provided at no cost.

Because long-term opioid drug injectors are at high risk of acquiring and transmitting HIV and other blood-borne infections, measures that reduce their drug use and risk of infection are critical to controlling the spread of these diseases. The conventional wisdom has been that paying for treatment provides a strong incentive to complete it. However, the NIH-funded study showed that treatment entry and retention is greater when free methadone maintenance treatment is offered, especially among injectors who have never tried treatment or who are reluctant to enter treatment. This study could have a great impact on governmental decisions on whether to provide free methadone treatment.

Another advance highlighted by the Working Group showed that the availability of good health care, even when used, may not lead to the desired improvements in health outcomes for patients with type 2 diabetes. The study surveyed various measures of health care availability and use, and the resulting health outcomes. Measures of health care availability and use included frequency of physician visits, health insurance coverage, screening for diabetes complications, and treatment for high blood sugar, high blood pressure, and abnormal lipid levels in the blood. Measures of health outcomes included high blood sugar, presence of protein in the urine, high blood pressure, and abnormal blood lipid levels. The study found that despite high health care access and utilization, health outcomes were poor. The Working Group emphasized that while the study shows that there is a great need for new and creative advances in care to increase the success of treatment, the study also shows that people should recognize that health is not generated primarily from illness care, but rather, is related to many other factors.

The Working Group acknowledged the importance of NIH-funded studies that consider the human responses of individuals who are exposed to the health care system in different ways. For example, the Working Group highlighted a study of family decision-making to withdraw life-sustaining treatments from dying family members. Decision-making with regard to end-of-life care is obviously emotional and stressful, particularly because it is not usually clear when life saving treatments become futile gestures that only decrease the quality of life. However, because many, if not most people eventually make such decisions, the availability of information that reduces the difficulty of these decisions is of widespread interest. The NIH-funded study showed that several factors increased the stress of decisions to withdraw support: the absence of an advance directive, being an ethnic minority, and having a long commute to the hospital. The Working Group noted that this is one of the first studies to demonstrate the value of an advance directive in easing the family's stress. Thus, by informing the decisions of those who anticipate end-of-life circumstances, or those who counsel them, this study could have a great impact on those going through such a difficult time.

Finally, the Working Group noted the importance of a study that developed a systematic framework for designing and evaluating the ethics of clinical research. Clinical research is critical to developing new methods for preventing, diagnosing, and treating disease. The new framework, which builds on the numerous regulations and codes that address the ethical conduct of clinical research, should provide a useful tool for clinical investigators, institutional review board members, and others in strengthening ongoing efforts to ensure that clinical research is conducted in an ethical manner and respects the rights and welfare of research participants.

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE ADVANCES**

- Alcohol Changes the Shape of Proteins
- Scientists Close in on Alcohol's Suspected Binding Site by Putting it in Overdrive
- A Mechanism of Alcoholic Liver Injury Identified
- Potential for Preventing Alcohol's Damage to Fetal Development
- Targeting Cellular E-mail: Alcohol and Potassium Channels
- Gene Knockout Points to Receptor's Role in Alcoholism
- Neurosteroids: A Newly Recognized Avenue of Alcohol's Action
- Mapping the Cocaine High Versus the Natural Reward High
- A Brain Chemical Found to Naturally Reduce Pain Responses
- The Role of Calcium in Establishing a Pregnancy
- Bone Marrow Stem Cells Can Be Made to Differentiate into Neurons
- A Gene Involved in Learning
- Abnormal Brain Pathways in Infants Who Die from Sudden Infant Death Syndrome
- The Link Between Formula Additives and Children's Intelligence
- The Effects of Intensive Reading Instruction on Brain Function and Reading Behavior in Children
- Rare Genetic Disease Sheds Light on Tumor Suppressor Gene
- Promising Target for New Drugs Against Malaria
- Biological Factor Found to Suppress Leukemia and Protect the Body from Infection
- Herpes Virus Hijacks Cell's Own Transportation System
- A New Target for Erectile Dysfunction Drugs
- Synthetic Antibacterial Molecule Kills Drug-Resistant Bacteria
- Key Enzyme Found Responsible for Abdominal Aortic Aneurysm
- Genetic Variation of  $\beta 2$  Receptor Affects the Response to Asthma Treatment
- Improving Understanding of the Genetics of Lymphangioliomyomatosis (LAM)
- Antibodies Can Promote Blood Clotting in Autoimmune Diseases
- Severity of Symptoms and Risk of Mortality Due to Hypertrophic Cardiomyopathy Varies with Location and Type of Mutations
- Human Pigmentation Disorder Linked to Genetic Defect in Inflammatory Pathway
- Environmental Response Gene Found to Have Important Role in Fetal Development
- Insight into Development of Important Immune System Components
- Fixing the Damage Done: Atomic Structure of a DNA Repair Enzyme
- New Subfamily of Environmental Response Enzymes Discovered
- Postnatal Sex Reversal of Ovaries – Insights into Estrogen Receptors
- Glutathione: A Real "Knock-Out" for Mammalian Development
- Control of Mitochondrial Iron Metabolism by Products of the Iron-Sulfur Gene Complex
- Folic Acid Binding Protein is Crucial for Mother to Fetus Folate Transfer
- Rendering the Brain More Vulnerable to Environmental Damage
- The Fidelity of DNA Synthesis by Human DNA Polymerase, a Skin Cancer Susceptibility Gene Product

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE ADVANCES**

- Hidden Conformational Epitopes of HIV Envelope Protein Identified
- New Study Increases Understanding of Imprinting
- Explaining the Death of Insulin-Secreting Pancreatic Cells
- Controlling Appetite Through Triglyceride Metabolism
- New Insights Gained into Genetics and Treatment of Polycystic Kidney Disease
- Hematopoietic Stem Cells Pave Way to New Treatments for Disease
- Insights into the Role of the Immune System in the Development of Type 1 Diabetes
- New Understanding of Insulin Receptors and Insulin Resistance in Type 2 Diabetes
- Insights into the Molecular Mediators of Hyperglycemic Damage to Blood Vessels
- Research on Nuclear Receptors May Aid Drug Development
- Genomes of Yeast, Worm, and Fly Aid Understanding of Human Disease
- The Feasibility of Large-Scale Mutagenesis and Phenotyping Programs
- A Genetic Linkage Map of the Baboon Genome
- MRI Reveals Changes in Brain Structure Associated with Multiple Sclerosis
- Application of Laboratory Research to the Development of a Therapy for Chronic Myelogenous Leukemia
- Predicting Lung Cancer by Detecting Methylated Genes
- Gene is a Critical Player in Tumor Metastasis
- Anti-Apoptosis Gene is Overexpressed in Cancer Cells
- Clue from Inherited Childhood Disorder May Help Explain Breast Cancer
- Chemokines in Multiple Sclerosis: Prospects for Better Drugs
- Mouse Model of Neurofibromatosis Developed
- Understanding the Early Steps in Neurodegeneration
- How Nicotine Causes Long Lasting Effects on the Brain
- The Normal Development of the Olfactory System is Dependent on Neuronal Activity
- Rapid Progress in the Mapping and Cloning of Genes Responsible for Hereditary Hearing Impairment
- The Molecular Biology of Taste Signal Transduction: Diversity Personified
- Obese Mouse Reveals New Approach to Building Bone
- Mice Reveal a New Target for Prevention of Bone Loss
- Correlation Found Between Genetic Defect and Appearance of Skin Disease
- Both Embryonic and Aging-related Genes May Regulate the Aggressive Behavior of Joint Lining Cells in Rheumatoid Arthritis
- Two Related Proteins Form a Physical Complex With Calcineurin to Regulate Gene Expression of Muscle Fiber Types
- Genes Express Differences in Tendon and Ligament Repair
- Research Yields Clues About the Cycling of Hair
- A Neuroendocrine Model Explains Gender Differences in Behavioral Responses to Stress
- Building a Brain Synapse: Understanding the Axonal “HOV” Lane
- A Newly Discovered Protein Transports A Major Excitatory Brain Transmitter
- Single Neurons Play Complex Roles in Encoding Memories

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE ADVANCES**

- New Views On Brain Development
- A Scout's Guide to Axon Guidance
- The Organization of Memories in the Hippocampus
- How Fear-Related Memories Are Stored – and Can Be Lost
- Experience and Biology Mold Capacity for Memory
- Imaging Shows the Brain is a Pictionary Plus
- Estrogen Increases Memory-Related Brain Cells in Adult Animals
- SLPI is Essential for Normal Wound Healing
- Cloning Resets the Telomere Clock in Cattle
- Genetically Mimicking Caloric Restriction Significantly Extends Yeast Life Span
- Use of Gene Expression Microarrays in Aging Research
- Extension of Average Life Span of Nematodes by Pharmacological Intervention
- Further Evidence that Presenilin-1 May Be One of the Major Amyloid- $\beta$ -Forming Enzymes
- Neuropathology in Mice Expressing Mutant Tau Protein
- Transgenic Mice Expressing Human Alpha Synuclein have Motor Impairment
- A New Model of Parkinson's Disease
- Mad Cow Disease: The Cause of Human Fatal Neurodegenerative Disease?
- New Neurotrophic Factor for Brain Cholinergic Neurons
- Study of Genetic Recombination in Malaria Parasite Will Lead to Localization of Virulence and Drug-resistance Loci
- Spotlight on Visual Proteins: Visual Protein Sees the Light of Day
- Seeing with Rewired Brains
- Neovascularization Associated with Age-Related Macular Degeneration
- Function of Osteonectin/SPARC in the Retina
- Scientists Identify Malaria Gene that Confers Resistance to Chloroquine
- Determination of the Crystal Structure of a Natural Killer Cell Inhibitory Receptor Engaging a MHC Class I Molecule
- Crystal Structure of Novel Protein Reveals New Treatment Target for Immune-Mediated Diseases
- Genes Provide Clues to TB Persistence
- Researchers Identify Ebola Virus Gene that Causes Massive Hemorrhaging
- Snapshots of Nature: Crystal Structure of an Interaction that Triggers Asthma and Allergic Diseases
- Novel Protein on Dendritic Cells Delivers HIV to T Cells
- Resting CD4+ T Cells are Not the Only Source of Resurgent HIV Virus Following HAART
- New Red Blood Cell Mutation Associated with Resistance to Malaria
- Sequencing the Mouse Genome: Providing Scientists with Tools to Interpret the Human Genome while Gaining Molecular Insight into a Powerful Model System
- Researchers Decipher the First Two Chapters of the Human Genetic Instruction Book
- Center For Inherited Disease Research: A Service to Help Researchers Identify Genes that Contribute to Human Disease



**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE ADVANCES**

- Mammalian Gene Collection: A Resource for Studying Gene Expression and Function
- Early Childhood Stress Predicts Vulnerability to Alcoholism
- Alcoholic Fathers' Behavior Predicts Intellectual Deficits in Their Children
- Children's Emotional Response to Alcohol's Scent on Parents
- Understanding the Immune System of HIV-Infected Adolescents
- "Nerve Sprouting" May Be Useful Target for Preventing Heart Rhythm Disturbances
- Maternal Immune Tolerance of the Fetus
- Mutations Within a Skeletal Muscle Gene Cause Genetic Muscle Disease
- The Assembly of Neural Circuits
- Sex Hormones Provide Clues to Development of Autoimmunity
- Extent of Viral Diversity Early in Hepatitis C Virus Infection Predicts Whether the Infection will Become Chronic
- Animal Model Shows Pain and Tissue Injury in Newborns Alters Nerve Circuitry and Reaction to Pain Later in Life
- Patterned Entry by Epstein-Barr virus in Polarized CR2-Positive Epithelial Cells
- Regulation of Nematode Life Span Through Sensory Perception
- Enteral Feeding Options Influence Corticosterone Patterns in Rats
- Effect of Female Gonadal Steroids on Stroke Injury
- Malaria Parasite Development in a Fruit Fly Model
- Alcohol Raises Risk of Brain Damage in Addicted Adolescents
- Smoking and Alcoholism: A Genetic Link?
- Craving for One Drug May Increase Cravings for Other Drugs
- Long-Term Behavioral Effects of Iron Deficiency Anemia in Infancy
- Treatment of Trichomoniasis Increased the Risk of Preterm Birth
- Dietary Sodium Intake Increases Risk of Cardiovascular Disease in Overweight Adults
- Improving Management of Asymptomatic Hyperparathyroidism
- Prolonged Beneficial Effect of Intensive Blood Glucose Control on the Complications of Diabetes
- Prevalence of Autoantibodies Against Contractile Proteins in Coronary Artery Disease
- Neural Circuitry of Emotion Regulation
- Understanding the Complex Genetics of Multiple Sclerosis
- Neurocognitive Phenotype in Turner Syndrome Mapped to a Critical Region of the X Chromosome
- Parkinson's Disease is Not Just a Brain Disease
- Understanding and Early Detection of Huntington's Disease
- Different Populations Have Different Rates of Total Hip and Total Knee Replacements
- Teen-Aged Girls With Juvenile Rheumatoid Arthritis Have Risk Factor for Osteoporosis
- The Influence of Stereotypes on Cardiovascular Health and Cognitive Functioning
- Mortality Continues to Decline in Industrialized Countries
- Environment and Not Heredity is the Overwhelming Contributor to Cancer Among Twins
- Early-life Childhood and Environment are Linked to Risk of Alzheimer's Disease

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE ADVANCES**

- Family Decision-Making to Withdraw Life-Sustaining Treatments from Hospitalized Patients
- Compare Preventive Interventions for Breast and Ovarian Cancer
- The Evolution of Bacterium-Human Interactions: The H. pylori Model
- Nitric Oxide Inhalation in Patients with Sickle Cell Anemia
- Improving Functional Disability in Nursing Home Residents with Dementia
- From Randomized Trial to Community-Focused Practice
- Activation of a Receptor Causes Abnormal Electrical Conduction in the Heart and a Lethal Heart Disease

**SCIENCE CAPSULES**

- Gene Knockout has Implications for Alcoholism Treatment
- Add Fruit Flies to the Search for the Genetics of Dopamine Response to Alcohol
- What Causes the Pleasurable Effects of Cocaine?
- Researchers Find Receptors for Molecules that Activate and Inhibit FSH
- Investigators Uncover How Substance Prepares Uterine Wall for Implantation
- Researchers Identify Gene for Sex Organ Development
- Maternal Gene Found to be Essential for Early Embryonic Development in Mice
- Uncontrolled Harmful Protein Formation
- Clues to the Development of Alzheimer's Disease
- Vaults: Hollow Barrels or Treasure Chests
- Inhibitor Protein Works by Changing Shape
- Structural Basis of DNA Synthesis
- Genetic Basis Found for Hypertension During Pregnancy
- Possible Explanation Found for High Levels of Hypertension in Black Americans
- Understanding the Genetics of Pulmonary Fibrosis
- Research on Rare Disease has Implications for Understanding Cancer and Normal Cellular Processes
- Identification of Protein Responsible for Ebola's Devastating Effects Lays Groundwork for Vaccine Development
- DNA Repair – Integrated and Multisteped
- Influence of Thyroid Hormones on Fetal Brain
- Prostate Cancer Predictor – Mutated Androgen Metabolism Genes
- Prostate Cancer – New Model for Studying Early Initiating Events
- Killing Cancer Cells
- Insight into Down's Syndrome – Possible Role of ITSN Protein
- Increasing Production of White Blood Cells – New Line of Investigation
- Inhibiting the Inflammation Leading to Rheumatoid Arthritis and Crohn's Disease
- Identification of a Gastrointestinal Tumor Suppressor Gene
- Simple System Yields Clues About Anemia

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE CAPSULES**

- AIDS Therapy May Promote Diabetes
- Regulation of Protein Degradation
- Prenatal Androgen Exposure May Affect Insulin-Glucose Balance in Adulthood
- Zebrafish Gene Sheds Light on Embryonic Development of Blood Vessels
- Animal Models of Neurological Disorders
- Mapping of a Gene for Severe Pediatric Gastroesophageal Reflux
- Molecular Motor Activity is Regulated by Its Load
- Tissue Engineering Shows Promise for Articular Cartilage Repair
- Establishment of Water Barrier of Skin Requires Coordination of Events
- Novel Melanocyte Protein is Discovered
- Monoclonal Antibody Identifies Hair Follicle Stem Cells
- Role of Measles Virus in Paget's Disease of Bone Begins to Emerge
- Chondrocyte Migration May Enhance Repair of Damaged Cartilage
- Aggrecanase Plays a Role in Cartilage Destruction in Arthritic Diseases
- New Neutrophil Types Identified
- Exit Signs Help Traveling Neurons in the Brain
- Why Prostate Cancer Homes to Bone
- Genomic Approaches to Understanding Oral Cancer
- Mutation of PAX9 is Associated with Oligodontia
- Productive Human Immunodeficiency Virus-1 (HIV-1) Infection of Epithelial Cell Lines of Salivary Gland Origin
- Impaired Osteoclast Function Produces Osteopetrosis
- Cell Transplantation and Aging
- Mutations in the BRI Gene Result in the Deposition of Amyloid and Consequent Dementia
- Dietary Restriction Increases Neurotrophic Factor Production in the Brain and Thereby Protects Neurons
- First Comparison of the Human Genome to a Complex Model Genome
- Data from the Human Genome Project Reveals Widespread Shuffling of Human DNA by LINE Elements
- Clue to the Mechanism of Latency in Ocular Herpes Infection
- New Images of a Major Lens Protein Give Insight into Protein Stability During Aging and Stress
- New Findings Help Explain How Patients with Glaucoma Lose Their Vision
- Development of Myopia
- The Genetic Basis of Stargardt Macular Dystrophy
- New Methods of Discovering Eye Tumor Genes
- The Nature of Activity in the Superior Colliculus
- The RPE65 Gene and the Visual Cycle
- Circadian Dependent Retinal Light Damage in Rats
- Discovery of Novel Mutation in BLNK Provides New Insight into B Cell Development

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE CAPSULES**

- Diesel Exhaust Particles (DEPs) Induce Allergic Antibody
- Discovery of New Pathway for Immune Recognition of Tuberculosis
- Genetic Mutation Linked to Missing Immunoregulatory Molecule
- Mutation Inhibits Proper Immune System Functioning
- Degradation of Defective Proteins Makes Antigens Available to Stimulate Immune Responses
- Identification of Protein Responsible for Persistence of Kaposi's Sarcoma -Associated Herpesvirus
- Discovering the Genetic Basis of Hearing Loss
- Longevity Genes
- Working With the Building Blocks of Life
- Elucidating the Role of Growth Factors in Embryonic Development
- Fruit Fly Genome Sequence will Provide Further Insights to Cancer and Aging
- Genetic Mutation Causes Common Defect in Early Development of Human Forebrain
- Cocaine High Related to How and How Quickly the Drug Reaches the Brain
- Marijuana Ingredient May Promote Tumor Growth
- Moderate Weight Loss OK for Overweight Moms Who Breast Feed
- Phospholamban Affects Contractility of the Heart
- Understanding Narcolepsy
- Pain Memories
- Obesity and Malalignment Correlate With Knee Osteoarthritis
- Exercise Results in Metabolic Shifts Lasting Several Days
- Molecular Mechanisms of Calcium Influx
- Changes in Physiological Response Characteristics of Cortical Neurons in Aging Primate Brain
- Changes in Diapered and Nondiapered Infant Skin
- Structural Characterization of Tear Components
- Plasma Membrane Cholesterol Release Modulates the Activation of Mammalian Sperm
- New Insights into the Natural History of Hepatitis C Virus Infection in Injection Drug Users
- Home Culture, Health Status Influence Infant Mortality Among U.S. Born Puerto Ricans
- Zidovudine Does Not Increase Adverse Pregnancy Outcomes
- Women's Fertile Days are Highly Unpredictable
- Psychosocial and Socioeconomic Factors Determine Who Stays in Long-Term Studies
- Presence of Rheumatoid Arthritis is Predictive of Development of Future Comorbidities
- New Insights into the Ethical Conduct of Clinical Research
- Quality of AMI Care for Medicare HMO Enrollees Equal or Better than for Fee-for-Service Medicare Recipients
- Cholesterol May Be a Modifiable Environmental Risk Factor for Alzheimer's Disease
- Parkinsonism and Cognitive Decline in Alzheimer's Patients
- The Sex Steroid, Testosterone, Modifies Working Memory in Elderly Men
- Attending to Cultural Language Improves Assessment of Symptoms
- Information for Cancer Patients

**Titles of NIH Research Outcomes Provided for Goal A:  
Add to the Body of Knowledge about  
Normal and Abnormal Biological Functions and Behavior**

**SCIENCE CAPSULES**

- Understanding the Experience of Sudden Cardiac Arrest
- Paths from Miscarriage to Depression
- Recruitment of Minorities as Research Subjects
- Caring for Patients in a Persistent Vegetative State
- Women’s Responses to Sexual Violence by Male Intimates
- The Island of the Color Blind
- Outcome for Hepatitis C Virus-Positive Persons is Better than Expected but Differences in Viral Clearance Exist Between Caucasians and African Americans
- Increasing Treatment Entry and Retention for Street-recruited Opioid Injectors: The Cost Factor
- Attention Deficit Hyperactivity Disorder and Substance Abuse
- New Reimbursement Classification System for Rehabilitation Care Recognizes Quality While Monitoring Costs
- Health Care is Not Related to Health Outcomes for Patients with Type 2 Diabetes
- Prostate Cancer Outcomes Study
- Estrogen Replacement Therapy and Breast Cancer Risk
- Risk of Bipolar Relapse with Lithium Discontinuation Increased in Post-Partum Period, But Not Pregnancy
- Behavior Modification for Urinary Continence

**STORIES OF DISCOVERY**

- Methamphetamine Abuse: Confronting a Public Health Crisis
- Looking in Cells for the Sources of Alcoholism
- Identification and Characterization of a Family of Bitter Taste Receptors
- Simian Immunodeficiency Virus Models the Human AIDS Virus
- The Speed of Sound – Motor Protein of Cochlear Outer Hair Cells Identified
- The Declining Disability of Older Americans
- Learning From Songbirds About Adult Brain Cell Generation
- Sequencing the Human Genome: Our Genetic Instruction Book
- A Century of Fruit Fly Research Sheds Light on Human Health and Disease
- Epidermolysis Bullosa: A Bedside to Bench to Bedside Story of Discovery
- Improving Treatments, Preventing Relapse: Atypical Antipsychotic Medications

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

### Performance Targets & Results

#### Annual Target

**Progress in developing new instrumentation or technologies that enhance capabilities for investigating biological functions and diagnosing and treating diseases and disorders.**

*FY 2001-2002 performance to be reported in February 2002 and 2003, respectively.*

#### FY 2000

*Performance: Target substantially exceeded. 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 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.*

#### FY 1999

*Performance: Target substantially exceeded. The Assessment Working Group concluded that FY99 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.*

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

**• Goal Background**

The development of new instruments and technologies is a key component of the success of the biomedical research enterprise. Improvements in the early detection of cancers, technologies to better visualize the living body in both normal health and disease states, and new ways to identify and target abnormal cells and tissues will provide a wealth of knowledge that can lead to new and improved diagnostics, treatments, and prevention strategies. Bioinformatics capabilities are providing the platforms to conduct complex analyses of data particularly in fields using genomic, proteomic, and imaging technologies and the means to more effectively communicate information to the research community and public.

Many of the advances in medical science today, including the mapping of the human genome, have been the result of the development of advanced technologies and instruments that permit investigators to explore the human body and open up new horizons for understanding development and disease. The continued progression of researchers to invent new instruments is vital to sustain the pace of medical discovery.

Instrumentation and technologies for the purpose of this review also include computers, computer programs, and databases. The information generated by researchers, the information needed to conduct clinical trials, and the information required for the optimal practice of medicine have long ago exceeded the capacity of pre-computer methods. Now it is essential that we continue to improve methods for archiving, analyzing, retrieving, and using new information in all the areas of biology and medicine. It is critical that we have the capacity to integrate the vast array of emerging genetic information into formats that are accessible to scientists worldwide, to establish new databases for visualizing 3-dimensional protein structures, to catalog the “molecular fingerprints” of genes that are turned on during the development of particular cancers, and to disseminate in a timely fashion critical information regarding public health and medical research.

A new emphasis on bioengineering brings new opportunities for advancing public health through the integration of non-medical sciences to create tools and technologies for biomedical applications. Research in biomaterials science, for example, expands our knowledge of how synthetic materials interact with body tissues, leading to development of new enhanced implantable devices, improved therapeutic procedures, and more accurate delivery of drugs to particular body sites. Research on acoustical, electrical, and magnetic field effects are now being applied in devices to aid visual and sensory perception. Research on imaging and signal processing have yielded instruments that have made it possible to scale up human DNA sequencing, which in turn transformed the way biotechnology and pharmaceutical companies approach therapeutic drug development. Development of nanotechnologies for sensing cellular and molecular regulation will provide new ways of detecting disease and response to therapies.

### ***Performance Assessment Approach***

#### *Basis and Data:*

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

The Working Group developed its assessment based on data provided by the ICs (science advances, science capsules, stories of discovery, and research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. (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 by the Working Group in assessing the outcomes of NIH research under Goal B in FY 2000 follow:

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 apply:

- ❑ 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 to biological functions and behavior, or new findings are not published/and or disseminated.



*Validation and Verification:*

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

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results***

Target substantially exceeded. The Working Group concluded that the research outcomes submitted for FY 2000 demonstrated that NIH had significantly contributed to progress in developing new or improved instruments and technologies and had fulfilled all the criteria (see *Performance Assessment Approach* above) for “substantially exceeding” the goal.

NIH’s Institutes and Centers submitted 59 science advances, science capsules, and stories of discovery (tabulated at the end of this section) that, in their judgment, demonstrated progress in developing new or improved instruments and technologies for use in research and medicine.

The 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. 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.

The Working Group underscored the importance that instruments and technologies have in enabling the development of scientific knowledge and that provide direct impact on human health. Several members commented that there had been a continuum of technology development related to science advances evaluated in FY 2000. An example of this was the continued technology achievements in cochlear implants. The speed at which technological advances are being made was also noted. Other reviewers acknowledged the rapid application of DNA array technologies and the payoffs that are being achieved provides evidence that NIH scientists are rapidly transforming ideas into laboratory tools and expanding their applications.

The Working Group also 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 there were potentially high payoffs in the form of breakthroughs, paradigm shifts, and expanded scientific applications.

**Research Outcomes and Their Significance**

The Working Group highlighted a number of especially noteworthy outcomes that demonstrated fulfillment of the assessment criteria for substantially exceeding Goal B.

## Genomics and Proteomics

The Working Group found that dramatic successes were being achieved in the evolution of instruments and technologies that are enabling researchers to take the next steps beyond the mapping of the human genome. Among the major advancements noted were the use of microarray tools that are being employed to measure changes in levels of gene expression in various cells and tissues. The DNA chip array concept that emerged in an NIH investigator's laboratory now enables investigators to evaluate thousands of genes in a single experiment. The Working Group noted prominent breakthroughs in applying DNA arrays to help explain mechanisms involved in several cancers, such as B cell lymphoma, breast cancers, and an aggressive form of cancer typically involving the skin called melanoma.

Other genomic advances that were featured included a new approach of using intronic (non-coding) portions of genomic DNA to assist in the inserting desirable genes into specialized viruses that are capable of correcting defects in human genes. The Working Group found that this basic research advance has the potential to address some of the technical barriers in currently existing gene therapy strategies. In addition, one member noted that this is an example of important high risk, high impact that NIH investments in gene therapy that will in the future pay off for approaches to treat HIV infection, immune system disorders, and cancer.

Reviewers also recognized other advances in genomic technologies that are occurring at a steady pace in measuring gene regulation in biological specimens. The Working Group noted the value of the advance citing the high-fidelity gene amplification methods to measure RNA in biological tissues. This advance provides evidence that NIH research exceeds the goal as it demonstrates a new research method that overcomes one of the limitations presented when an insufficient amount of biological material precludes the use of DNA amplification techniques. This is of special importance in the evaluation of patients receiving bioimmunotherapy. This advance provided evidence of overcoming a technical barrier that previously precluded some crucial biological questions from being pursued. The Working Group placed high value on genomics technologies recognizing their potential future application as diagnostic and therapeutic monitoring approaches.

Working Group members noted exciting advances in the basic biological techniques used to understand key roles that proteins serve in biology. One advance that was featured as evidence for surpassing the criteria for Goal B was the application of robotics to monitor interactions of proteins within yeast cells. Normal biological processes involve hundreds to thousands of biochemical interactions of proteins in normal cellular pathways that regulate vital functions of the organism. For many years, scientists have been challenged by studying multiple interactions of these types, and the use of robotics now makes large scale monitoring possible. This science advance was also recognized to have implications for genome-wide screening of critical protein-protein interactions that may ultimately be applied to diagnostic measures and drug development platforms. Such applications in yeast will likely be expanded to other types of cells and enable detection of abnormal protein function in diseases such as diabetes, cardiovascular disease, and cancer. One member noted that this advance was an encouraging sign of expanded use of robotics in medical sciences building on research advances reported in

last year's review that featured a science advance about robotic recording of intracellular calcium interactions.

Other science advances included the combination of mass spectrometry, light microscopy, and electron microscopy for the elucidation of critical protein structures. The example cited was the use of this combined approach to resolve the protein structures of vital cellular components that previously had perplexed scientists using standard approaches. In this research, scientists were able to identify all of the key protein elements of the nuclear pore complex of yeast cells that regulates the transport of large molecules in and out of the nucleus of the cell. The reviewers recognized the potential for this combination technique to be utilized in the resolution of other key proteins in cell structures and in therapeutic development. Reviewers also noted the potential implications of the science advance that describe the use of refined mass spectrometry methods to elucidate the full length structure of membrane-bound proteins in bacteria. Previously, membrane-bound proteins were very difficult to resolve in their full length leaving scientists with incomplete pictures of their structure. Now the use of rapid chromatographic separation coupled with spectrometric analysis provides an approach to circumvent this barrier to determining critical protein structures.

Reviewers also cited the science advance of an application of flow cytometry to recognize DNA fingerprints of bacteria. This method provides a rapid, low cost means of distinguishing normal bacteria from those that are harmful, such as *E. coli*. The extended applications for this technique in food safety, environmental health, and infectious disease monitoring were cited as examples of how NIH research exceeded the goal by applying technologies to address new problems.

### Information Technologies

The Working Group expressed interest in the use of information technologies in genomic applications because of the large amount of information being generated and its importance to future advances in biomedical research. In particular, they cited the example of the science advances describing the database of human single nucleotide polymorphisms (SNPs) being developed. SNPs represent the genetic basis of individual variation in normal and abnormal biological functions including inherited monogenetic diseases and susceptibility to complex diseases. Researchers are applying these genetic understandings to understand normal and abnormal structure and function contributing to variation in human biological responses and in some cases the disease process itself. This information has been useful in developing SNP maps that are already enabling target-specific drug development strategies. Several members of the group commended the collaboration among the NIH and private research investigators involved in this research project. The development of a public database will enable all researchers access to a rich discovery platform for targeting specific therapies for individuals. Overall, the Working Group recognized as important several science advances that described the value of public databases as research tools.

Other key internet-based resources were lauded by the Working Group for enhancing researchers' ability to analyze large data sets of genomic information. One example is the development of computer analysis tools, such as the CONCORD algorithm that when coupled

with radiation-hybrid maps of genes were viewed as an important navigation approach for researchers searching for critical disease genes. Several members commented one of the conundrums in science resulting from rapid advances in technologies to generate genomic information is the emergence of complex analytical challenges. They cited the importance of applying computer science and mathematical approaches to develop the LocusLink and RefSeq databases that help researchers archive and retrieve genomic information that is annotated with descriptive information about what is known about the function of the genes they represent.

The Working Group also concluded that NIH-sponsored information technology resources were being used to effectively communicate important concepts about science and medical information to the public. One example that they cited is the science advance describing a website called *Profiles in Science* that highlights the research careers of 20<sup>th</sup> century biomedical scientists. This resource provides students, teachers, and researchers with readily accessible historical perspectives on research careers dedicated to scientific discovery. Several participants noted that this resource was a valuable way for NIH to inform young people about career opportunities and was an important step to assuring that a vibrant research workforce is being prepared for future biomedical research challenges. Another example of NIH investments in information technologies that spans the research community and the public is the on-line database listing all government-sponsored and many privately sponsored clinical trials. This resource is a valuable one-stop shopping site that provides general information about health and clinical trials. Recent data indicate that [clinicaltrials.gov](http://clinicaltrials.gov) is one of the most highly accessed websites in the government and the Working Group noted that this was additional evidence that NIH had exceeded the criteria for Goal B.

Other participants indicated the value of the next generation Internet implementation that would serve expanded application of the Visible Human datasets. This is now providing interactive 2- and 3-dimensional visualizations of the structures of the human body. One implication of this technological advance is that it now opens the door for visualization beyond organs and tissues to individual cellular structures. Another Internet application that some felt had immediate practical application in human health was the evolution of an internet-based archival and network infrastructure to support digital mammography. Important components of this NIH research advance is the development of an integrated system that allows scientists and physicians near instant access to breast screening images in a secure site that protects confidentiality of medical information. Other Working Group members cited that the advances in computer-based technologies to aid in the development of cancer treatment strategies for remote regions of the country and beyond. This was cited as an example of the use of technology to break down distance barriers in ensuring patients in rural settings access to high quality clinical research protocols.

#### Innovative Imaging Tools and Applications

The Working Group recognized a substantial portfolio of imaging tools and applications that were yielding important outcomes. Several members found a science advance on the use of virtual colonoscopy to be particularly important as it provides future noninvasive means for early detection of polyps in the colon as a cancer prevention strategy. This advance features the development of computer-based analysis of computerized tomographic (CT) scans that allows

interpretation of a large number of images and provides the practical benefit of patients potentially avoiding the discomfort of conventional invasive colonoscopic procedures. One member noted that patients often delay cancer screening because of personal discomfort and this new approach offers a potential option to counter the resistance threshold that prevents many from undergoing crucial cancer screening. Other members were equally enthusiastic about the potential widespread medical applications of this technology but recognized that patients with polyps identified by this method would ultimately require a standard colonoscopic procedure. Others also noted the need for future cost-effectiveness studies of virtual colonoscopy compared the conventional method.

Laser scattering spectroscopic methods were identified for their potential use in early cancer detection. The major advance with this new method was cited as its real-time visualization properties that allows investigators to identify precancerous cells of internal tissues of the body organs, such as the urinary bladder and cervix, and in some cases without the need for biopsy. Optical coherence tomographic applications were cited in the employment for measuring optic nerve measurements in early detection of nerve damage in glaucoma patients. Building on past advances in vascular diseases, the use of magnetic resonance imaging is showing higher resolution of “vulnerable” plaques in coronary arteries. Researchers have refined a method to “black out” the motion of blood flow inside vessels that allows high resolution detail imaging of plaque composition to determine those that are most likely to rupture and cause a heart attack. Several members of the Working Group featured the early diagnostic potential of this technique in asymptomatic patients and the application in other types of vascular diseases as evidence of exceeding the evaluation goals.

Other members noted an application of magnetic resonance imaging for physiological applications was an exciting new use of imaging tools. This science advance featured the high resolution images of the extraocular muscles provided key insights into muscle control of eye movement. They felt that this technique will likely be used in preparing for surgical approaches to treat disorders of muscle strength and control such as strabismus. Imaging techniques are also helping investigators take major strides in understanding brain chemistry and neuropharmacology. One member cited the use of single photon emission computed tomography (SPECT) imaging applications in animal models to visualize the binding of a new compound to specialized serotonin transporters in the brain. This new use of SPECT is opening doors for noninvasive studies to potential candidate therapies for mental health disorders.

The Working Group noted several scientific advances in the area of improvement in hearing technologies that built on advances that were featured in the FY 1999 assessment. The Working Group noted that these technologic advances were having impact on both extremes of ages, the very young with congenital deafness and in older populations with acquired hearing loss. The reviewers cited advances in nanofabrication techniques as one basis for improving the quality of sound resolution and recognition. Improvement in quality of life via the translation of basic research in these technologies was highlighted by the group as one of the justifications for the portfolio to have exceeded Goal B.

The Working Group also endorsed several of the science advances about imaging technologies and applications included in Goal D as evidence that NIH research had exceeded the criteria of

Goal B. These included the discovery of a new probe in animal models that was shown to detect highly specific biological markers in senile plaques characteristic of Alzheimer's disease in animal models. This probe may open the door for noninvasive imaging strategies for early detection of this devastating neurological disorder. Another example is the noninvasive functional imaging being used to measure brain oxygen levels in adults and critically ill newborn infants. Among the advantages of this technique using near-infrared light is the detection of fluctuations in oxygen on a continuous basis without having to perform painful skin punctures to obtain blood samples. One member of the review group noted that noninvasive near-infrared technologies were now being exploited in other noninvasive biomedical areas by the medical device industry. Reviewers noted these as additional examples of how NIH research exceeded Goal B as evidence of instruments are novel approaches to answering important biological questions and improve quality of life by reducing discomfort as noninvasive techniques provide painless approaches to obtaining vital biological data.

**Titles of NIH Research Outcomes Provided for Goal B:  
Develop New or Improved Instruments and Technologies  
for Use in Research and Medicine**

**SCIENCE ADVANCES**

- The New Immigrant Study: Understanding the Background, Skills, and Impact of Immigration on U.S. Society
- The Mouse Intracytoplasmic Sperm Injection Model: No Adverse Effects of Bypassing Conventional Sperm Formation and Fertilization
- Robots Eavesdrop on Cellular Discussions
- Targeted DNA Insertion May Aid Gene Therapy
- Simple Breath Test Predicts Gene-Linked Drug Response
- Laboratory-Grown Heart Valves Show Potential as Valve Replacements
- Clinical Study Shows That New Treatment May Improve Feasibility of Bone Marrow Transplantation
- Development of a Novel Technique To Analyze Membrane Proteins
- A Useful Technique for Understanding Signaling in the Cell
- Genome-Wide Screening of Protein Interactions
- Fingerprinting Bacteria
- Identifying the Function of Proteins
- Most Common Type of Non-Hodgkin's Lymphoma is Actually Two Diseases, Powerful New Genetic Analysis Tool Reveals
- Isolation, Purification, and Multiplication of Adult Neural Stem Cells
- Cochlear Implants
- Early Identification of Hearing Impairment
- Development of a High-fidelity Gene Amplification Method Allows Quantitative Measurements of Biological Functions Using Minimal Amounts of Living Tissues
- “Virtual Colonoscopy” One Step Closer to Routine Clinical Use
- Magnetic Resonance Angiography Displays Small Vessels Without Invasive Catheterizations
- Improved Integration of Data from Multiple Gene Maps Leads to Better Localization of Human Genetic Markers
- LocusLink and RefSeq Databases Simplify Integrated Retrieval of Genomic Information
- ClinicalTrials.gov
- Profiles in Science
- Development of a New Technique for Examining Different Structures in the Eye
- Development of a Multimedia Educational Tool about the Human Genome and Genetics for Students and the Public
- Accumulation of Cellular Iron: A Likely Culprit in Degenerative Diseases of the Nervous System
- A Simple, Inexpensive Method for Determining Prognosis in B Cell Lymphocytic Leukemia
- How Cells Engineer Connective Tissue Matrix
- New Genetic System for Following Cranial Neural Crest Cells in Mice
- Early Warning System is Discovered to Fight Infections and Cancer
- Imaging Technique Reveals Changes in Brain Structure
- Advances in Ocular Kinematics

**Titles of NIH Research Outcomes Provided for Goal B:  
Develop New or Improved Instruments and Technologies  
for Use in Research and Medicine**

**SCIENCE CAPSULES**

- Fluorescent Brain Cells Help Track Master Reproductive Hormone
- Detailed Images Achieved with New Magnetic Resonance Imaging (MRI) Technique
- Improved Prospects for Gene Therapy Requiring Large Genes
- New Method to More Quickly Study Cellular Regulatory Processes
- Automatable Method for Protein Identification
- Efficient Production of Dopamine Nerve Cells
- Hearing Aids
- Altruism Motivates Participation in Schizophrenia Research
- Assuring Safe Feeding Tube Placement
- A Database of SNPs Will Shed Light on Human Variation and Disease
- A New Method for Searching for Patterns in Proteins
- Complete Genome Data for More Than 700 Organisms Facilitates Comparative Analyses
- Next Generation Internet Implementation to Serve Visible Human Datasets
- Remote Treatment Planning System
- Mammography for the Next Generation Internet
- Multilateral Initiative on Malaria
- Tribal Connections
- Internet Connectivity Performance Evaluation
- New Imaging Instrumentation for Diagnosis of Eye Diseases
- Intranasal Administration of Naked TGF- $\beta$  DNA May Be Used to Treat Inflammatory Diseases
- Early Detection of Cancer Cells
- Novel SPECT Ligands to Image the Serotonin Transporter in Human Brain
- New Technique Eliminates a Step in Making Genetically-Altered Mice
- RNA Interference: A New Method for Controlling Gene Expression

**STORIES OF DISCOVERY**

- MEDLINE and MEDLINEplus: A Continuing Story of Discovery
- Genome-scale Analyses: cDNA and Tissue Chips
- Single Nucleotide Polymorphisms (SNPs): New Tools for Tracing Inherited Diseases



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

### Performance Targets & Results

#### Annual Target

**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.**

*FY 2001-2002 performance to be reported in February 2002 and 2003, respectively.*

#### FY 2000

*Performance: Target substantially exceeded. 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.*

#### FY 1999

*Performance: Target successfully met. 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.*

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

### ***Goal Background***

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 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 transmission by lowering the concentration or viability of the infectious agents. Other drugs may reduce the progress or severity of inherited disease or disability when taken by individuals with low-level or presymptomatic 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.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

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

The Working Group developed its assessment based on data provided by the ICs (science advances, science capsules, stories of discovery, and research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. (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 by the Working Group in assessing the outcomes of NIH research under Goal C in FY 2000 follow:

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

- ❑ 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 results 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 to biological functions and behavior, or new findings are not published/and or disseminated.

#### *Validation and Verification:*

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.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

Target substantially exceeded. The Working Group unanimously concluded that the research outcomes submitted for FY 2000 represented a significant contribution to progress in developing new or improved approaches for preventing or delaying the onset of disease and disability and

fulfilled the criteria (see *Performance Assessment Approach* above) for “substantially exceeding” Goal C.

NIH’s ICs submitted 101 science advances, science capsules, and stories of discovery (tabulated at the end of this section) that, in their judgment, demonstrated progress in developing new or improved approaches for preventing or delaying the onset of disease and disability.

The Working Group agreed that of all of NIH’s outstanding preventive efforts, advances in AIDS prevention, particularly in the prevention of mother-to-child HIV transmission, stood out for their broad health effects. The Working Group emphasized that NIH’s advances in this area should be viewed as a model for the development of highly successful preventive measures through the integration of basic research and behavioral science. The Working Group believed that even if there had been no other NIH advances in the area of prevention, NIH would have substantially exceeded the goal. Group members stressed the need to repeat this highly successful coalescence of advances in basic biology and behavioral strategies in other areas, such as the prevention of drug addiction and violence.

While the Working Group unanimously concluded that NIH had substantially exceeded Goal C, they also noted they were aware of many impressive advances in prevention, particularly in the area of vaccine development, that are not represented in the assessment materials. In addition, the Group emphasized the need to strengthen NIH-supported preventive research, particularly in the areas of environmental exposure to deleterious chemicals, alternative medicine, infectious diseases, and prevention of violence. They stressed the importance of integrating discoveries in genetics with appropriate behavioral interventions. And, they stressed the importance of eliminating health disparities as key to the continued success of NIH’s research efforts in the area of prevention.

## **Research Outcomes and Their Significance**

The Working Group highlighted a number of specific research outcomes that they judged to be especially noteworthy and discussed the significance of these types of findings.

### Preventing HIV Transmission

The Working Group noted that in the area of AIDS prevention, NIH-funded research on behavioral as well as pharmaceutical and other preventive methods has resulted in significant reductions in morbidity and mortality. Indeed, it is clear that if these effects on human life and health could be reduced to financial terms, the benefits of NIH-funded research in this area alone would far outweigh the cost of all other NIH expenditures.

The developments in the prevention of HIV transmission highlighted the progression of advances in basic research to the development of practical preventive measures. For example, the Working Group emphasized the link between improved understanding of heterosexual transmission of HIV from basic studies such as one that shows that a specific protein on the surface of certain vaginal cells contributes to infection by transmitting HIV to the lymph nodes,

and applied studies that aim to prevent transmission through the development of microbicides that inactivate or kill pathogens such as HIV. The need for such microbicides is particularly urgent, because it has been shown that nonoxynol-9, a spermicide that was thought to block transmission because it inactivates HIV in a test-tube, actually facilitates sexual transmission of HIV. However, recent NIH-funded studies have demonstrated the safety of novel microbicides, one developed from an extract of seaweed, and the other from a gel that maintains the normal acidity of the vagina. These findings may lead to major advances in preventing the transmission of HIV.

Another NIH-funded advance that has contributed to the prevention of transmission of HIV is the development of combination drug regimens known as highly active antiretroviral therapy (HAART). Recent studies have shown that HAART not only improves the health of the individual by minimizing damage to the immune system, it also prevents transmission of HIV by reducing viral load. NIH-supported scientists have shown a direct correlation between the concentration of HIV in the blood and the rate of sexual transmission. This finding emphasizes the need to develop low-cost, practical methods for reducing viral load, particularly for use in countries where the epidemic is escalating and financial resources are limited.

NIH-funded research also contributed to a dramatic reduction in mother-to-child HIV transmission. Mother-to-child HIV transmission occurs both during pregnancy and labor, and later during breastfeeding. Like sexual transmission of HIV, mother-to-child transmission during pregnancy and labor is related to viral load. Thus, in the U.S. and developed countries, it has been possible to reduce perinatal transmission to as little as 4-6% by providing antiretroviral drug therapy to the mother during pregnancy and labor, and to the newborn following birth. Delivery by cesarean section, which has similar rates of complications in HIV-infected and uninfected women, further reduces the transmission rate to 2% or less. However, the cost and complexity of standard drug treatments and cesarean section are major barriers to using these measures to prevent perinatal transmission in the developing world. Accordingly, NIH-funded scientists have developed short-term or even single-dose antiretroviral therapies that are nonetheless very effective in reducing perinatal transmission and may prevent HIV infection in over 250,000 children born each year.

Despite this success, the results of NIH-funded research illustrate the barriers to effective HIV-prevention efforts in the developing world. Breastfeeding, the social, cultural, and economic norm in many resource-poor countries, is a major factor in the transmission of HIV from mother to child. Thirty-seven percent of infants who are breastfed become infected, compared to only 21% of those receiving formula. Nonetheless, in NIH-supported clinical trials in the developing world, 70% of the women who were provided formula to feed their infants nonetheless chose to breast feed. These findings illustrate the need to develop ways of changing longstanding cultural and behavioral patterns that contribute to the transmission of HIV.

#### Preventing Other Infectious Diseases

The Working Group noted that the materials for Goal B described several studies that provide a basis for developing vaccines against infectious diseases. For example, several NIH-funded studies may contribute to the development of vaccines against urinary tract infections, which are

usually caused by the bacterium *Escherichia coli*. NIH-supported researchers found that a molecule on the surface of *E. coli* cells mediates the binding of the bacteria to bladder cells, and is essential for the entry of the bacteria into bladder cells. Monkeys vaccinated with this molecule produce antibodies to it, and do not develop infections when challenged with *E. coli*, suggesting that such vaccination confers protective immunity. In addition, researchers showed that certain other compounds block the uptake of the bacteria into mast cells, which mediate allergic responses. These studies on the molecular mechanisms of *E. coli* infection provide a basis for developing preventive measures for urinary tract infections.

Other NIH-funded studies suggest a two-pronged approach to preventing otitis media, a middle ear infection that is common in children. Researchers who studied twins and triplets showed that although otitis media is an infectious disease, susceptibility to it is largely inherited and can be amplified by environmental conditions, such as parental smoking. With this knowledge, physicians will be able to identify high-risk relatives of patients with otitis media, facilitating early detection and treatment. Eventually, scientists may develop DNA diagnostic tests to identify susceptible individuals. In addition, NIH-funded scientists are developing a vaccine for unencapsulated *Haemophilus influenzae*, one of the bacteria that causes otitis media. This vaccine has been shown to be safe in adults, and has protected against infection in animals.

NIH-funded researchers have also made progress in developing a vaccine against malaria, a deadly tropical disease that kills over 1 million people per year. Specifically, the researchers have shown that certain antibodies can prevent the parasites that cause malaria from binding to red blood cells. These antibodies block certain receptor proteins that facilitate binding and invasion of red cells by the malaria parasites. The experiments are a first step toward developing vaccines that work by eliciting immune responses to the parasite receptor proteins.

Finally, studies by NIH-funded scientists have shown how to prevent drug-related damage in acute gastrointestinal illness in children. About 15% of children with gastrointestinal infection caused by *E. coli* O157:H7 develop hemolytic uremic syndrome, which can cause kidney failure and even death. The researchers found that children treated with antibiotics during this illness actually had a higher risk of developing hemolytic uremic syndrome, possibly due to the release of toxins by the dying bacteria. Accordingly, it is very important that physicians not prescribe antibiotics to treat children with acute gastrointestinal illness.

#### Preventing Alcohol and Drug Abuse and Abusive Behavior

The Working Group agreed that NIH-funded research is making significant contributions to the prevention of alcohol and drug abuse and related injuries. For example, alcohol abuse is the most common contributing factor for injury in the U.S.; about half of the patients admitted to trauma centers are under the influence of alcohol. Because a recent life-threatening injury may make patients more receptive to alcohol counseling, NIH-supported scientists studied whether a “brief intervention”—a single 30-minute interview with a psychologist following an alcohol-related injury—can significantly reduce alcohol dependence and abuse. After 12 months, the intervention group had 47% fewer injuries than did the control group. Moreover, those in the intervention group had a decrease in alcohol consumption more than three times that of the control group (22 vs. 7 standard drinks per week). This decrease in alcohol abuse should prevent

many alcohol-related injuries. Other studies addressed the value of interventions in preventing drug abuse. For example, one study found that schools could be effective in engaging families in prevention efforts during high-risk periods for adolescents, such as the transition from elementary to middle school.

NIH-funded research on gender and ethnic differences in the ways that drug use and abuse develop will also improve drug abuse prevention efforts. One study examined the situations in which 2,500 African American, Mexican American, and European American youths encountered drugs and their reactions to drug offers. Ethnicity and gender differences in the frequency and venue in which individuals encountered drugs—such as from family members or acquaintances, or at homes, parties, or on the street, emerged. However, all groups exhibited little skill in resisting drug offers. This study will improve and inform drug abuse prevention efforts.

### Preventing Alzheimer's Disease

In this area, the Working Group focused on several noteworthy studies that will improve the ability to predict risk for Alzheimer's and identify early, equivocal Alzheimer's cases. In these studies, NIH-funded scientists developed advanced magnetic resonance imaging techniques and used them to predict which patients with memory impairment would develop Alzheimer's. Thus, these imaging techniques may be very useful in targeting preventive measures and therapies before the onset of debilitating disease. The Working Group also commented on a recent NIH-funded study that examined the utility of a nasal spray of amyloid $\beta$  as a means of inducing antibody-mediated removal of amyloid plaques, as has been demonstrated to occur in response to vaccination by injection of amyloid $\beta$ . The study showed that the nasal spray is promising as an approach to preventing Alzheimer's disease, and may be more easily administered and better tolerated than an injectable vaccine.

### Preventing Obesity, Diabetes, and Cardiovascular Disease

In this area, the Working Group highlighted outstanding advances stemming from research on behavioral modifications as well as on genetic and molecular mechanisms. The Group commented on a promising NIH-funded study in which the researchers developed a sensitive assay for anti-insulin autoantibodies present in the blood of infants with a high risk of developing diabetes. This assay will permit public health screening of infants for diabetes risk, and the targeting of preventive therapies when they become available. In addition, the Group highlighted a study that extended our knowledge about leptin, a hormone involved in the regulation of food intake and the control of body fat accumulation. The study showed that a variant in the leptin receptor gene is associated with higher fat levels in middle-aged white males. This finding may be an important step in developing preventive and therapeutic strategies.

The Working Group also commented on the number and effectiveness of studies that aimed to prevent obesity, diabetes, and cardiovascular disease through the use of easy-to-adopt changes in behavior, such as increased physical activity. These studies involved children, adolescents, adults, and the elderly. Two particularly noteworthy studies examined methods to prevent the alarming increases in obesity in children and adolescents that have been noted in recent years.

Based on widespread speculation that television and video games contribute substantially to the increase in obesity, one NIH-funded study examined the effect of an intervention to decrease media use among third- and fourth-grade students. The intervention consisted of 18 lessons incorporated into the classroom curriculum during a six-month period. The lessons were designed to motivate children to reduce the time they spent watching television and playing video games. The lessons were followed by 10 days of no television, followed by a period of limited television and video game use. Although compliance was not perfect, students in the intervention group had statistically significant decreases in body mass index and other measures of body fat. Thus, these readily adopted lessons may be a promising approach to preventing childhood obesity.

However, another study found that physical activity is not the only factor that contributes to obesity in adolescents. Rather, the effect of physical activity depends on ethnicity, gender, and socioeconomic status. African American adolescents and female adolescents of low socioeconomic status have a greater risk of being overweight, regardless of their reported physical activity and television viewing. However, the study found that participation in high-intensity exercise protected boys who watch more than two hours of television per day from being overweight. By contrast, participation in high-intensity physical activity had no effect on weight control in girls. The strong relationship between weight and ethnicity and socioeconomic status pointed to the importance of aiming weight control programs at those in high-risk groups.

Because obesity and reduced physical activity are major risk factors for the development of type 2 diabetes, another NIH-funded study examined the effect of different levels of physical activity on the risk of type 2 diabetes in women. The study concluded that the greater the overall activity level, the greater the reduction of risk of type 2 diabetes in women. Short periods of vigorous activity were equivalent to longer periods of moderate activity, such as walking. This finding is of considerable importance, because walking is the most common physical activity in middle-aged and older people, and carries the least risk of injury. Moreover, another NIH-funded study showed that walking and other low-intensity exercise programs can be initiated by most older persons without a prior exercise stress test.

Exercise is also important for men, particularly those who are obese, in reducing the risk of cardiovascular disease. NIH-funded researchers examined the effect of cardiorespiratory fitness, a measure of exercise capacity, on the risk of death from cardiovascular disease in normal-weight, overweight, and obese men. In all groups, "fit" men had a lower risk of death from cardiovascular disease. Indeed, fitness seems to counteract the risks associated with obesity, since obesity did not increase the risk of death among the fit men.

Finally, the Working Group noted the value of an NIH-funded study that compared the effectiveness of new, expensive anti-hypertensive drugs with less expensive drugs that have been on the market for some time. Although it had been previously demonstrated that the newer drugs are very effective at controlling blood pressure, their ability to reduce cardiovascular events such as heart attacks was unknown. In a large clinical trial, the NIH-funded researchers demonstrated that an inexpensive diuretic is superior to the newer, more expensive alpha-adrenergic blocker in its ability to prevent heart attacks and congestive heart failure. Thus, this study indicates that physicians should prescribe the diuretic to prevent cardiovascular events.



### Preventing Cancer

The Working Group pointed out the importance of a study of the legacy of diethylstilbesterol (DES), a synthetic estrogen that previously was used to prevent miscarriages, but is now known to cause a rare vaginal cancer in the daughters who were exposed to the drug *in utero*. New studies by NIH-funded researchers used laboratory mice to examine the effects of DES, because they mature rapidly and can be used to demonstrate multigenerational effects within a short time. These studies showed that the sons of the daughters exposed to DES (“DES grandsons”) are also affected, even though these mice were never exposed to DES. The DES grandsons developed tumors in the testis and reproductive tract. These studies will alert physicians to closely monitor the sons of DES daughters, so that deaths from these rare cancers can be prevented.

The Working Group also highlighted the importance of a study that showed that nearly 85 percent of patients undergoing traditional cancer therapy also use complementary and alternative medicines (CAMs). In some cases, herbs and vitamins may interact with traditional therapies, masking or distorting their effects. This study underscores the need for better patient-provider communication so that such counterproductive interactions can be avoided.

### Pregnancy and Child Health

The Working Group discussed a number of outstanding studies designed to develop or implement preventive measures addressing diseases or disabilities acquired by children during pregnancy or early childhood. In one such study, NIH-funded researchers discovered a way to predict whether a pregnant woman is at high risk for spontaneous preterm birth. In that study, the researchers identified a protein, fetal fibronectin, that is present in high concentrations in the vaginal secretions of women at risk for preterm delivery. In addition to its predictive value, the discovery may provide insight into the reasons for spontaneous preterm delivery, which is the leading cause of infant morbidity and mortality. The Group also commented on a study that showed that maternal smoking during pregnancy is associated with behavioral problems in two-year-olds. While the study did not identify the mechanism by which smoking caused the behavioral problems, it provided yet another incentive for mothers to avoid smoking during pregnancy.

The Group also commented on an NIH-funded study that showed that a video series developed for new parents had a significant effect on infant health. The video, “My Baby U,” was designed to give new parents accurate information about infant health and development. Infants whose parents viewed the video series experienced fewer severe illnesses and required far fewer medical services than those whose parents did not see the video. Thus, the video is an example of another simple behavioral intervention that is very effective in preventing disease.

**Titles of NIH Research Outcomes Provided for Goal C:  
Develop New or Improved Approaches for Preventing or Delaying  
the Onset or Progression of Disease and Disability**

**SCIENCE ADVANCES**

- Alcohol Interventions in Trauma Centers: Reducing the Risk of Repeat Injuries
- Successful Prevention Program Targets Steroid Abuse in High School Athletes
- School-based Program Reduces Smoking Among Minority Girls
- New Approaches to Preventing Drug Abuse
- Programs Can Bring About Positive Behavior Changes Among Youth Living with HIV
- Understanding Critical Gender and Ethnic Differences in Pathways to Drug Abuse Improves Prevention Efforts
- Smoking During Pregnancy May Increase the Risk of Behavioral Problems in Children
- A New Product That May Prevent HIV Transmission Enters Clinical Trials
- Mathematical Model May Help Reduce Antibiotic Resistance
- Study Sheds New Light on Genetic Predisposition to Obesity
- Molecular Snapshot of Pain and Inflammation Initiation
- Role of Diet and Genetic Mutation in Preventing Lung Cancer
- From Mother to Daughter to Grandson - The Legacy of DES
- Effects of Dioxin on Gender Ratios in Offspring of Exposed Men
- How Lead Exposure May Work to Damage the Developing Brain
- Urinary Tract Infections: Identification of Molecular Mechanisms of Infection
- Mechanisms of Chromosome Missegregation in Cancer Cells
- Advanced Imaging Technique Helps Predict Risk for Alzheimer's Disease
- Early Expression of Anti-insulin Autoantibodies of Humans and the NOD Mouse: Evidence for Early Determination of Subsequent Diabetes
- Daily Smoking Not Necessary for Nicotine Dependence in Young People
- Noise Induced Hearing Loss
- Strong Genetic Component to Otitis Media
- Minor Variations in a Gene for a Bone Protein Lead to Lower Bone Density
- Low Calcium Intakes and Absorption Contribute to Increased Fracture Risk in the Elderly
- Gene Found for Papillon-Lefevre Syndrome - A Disorder Affecting Skin and Gums
- Nasal Administration of Amyloid  $\beta$  Can Reduce Brain Amyloid  $\beta$  Deposition
- Fitness Affects Mortality Risk Regardless of Fatness
- Inadequate Treatment of Hypertension and Atrial Fibrillation in the Elderly
- Identifying Gene Variants Affecting Disease Risk Factors and their Interactions with Exercise
- Natural Killer Cell Activity and Resistance to Tumor Metastasis
- Influence of Physical Activity, Socioeconomic Status, and Ethnicity on Weight in Adolescents
- Eligibility for Managing Childhood Dehydration in Alternative Settings
- Coping Skills Training for Youth with Diabetes Mellitus
- Early Intervention to Improve Maternal and Infant Outcomes
- Long-Term Management of PMS Symptoms Using Nonpharmacological Interventions
- Description of Herpes Simplex Virus Movements in Nerves May Lead to New Treatments
- Gene Therapy for Sight-threatening Uveitic Disease

**Titles of NIH Research Outcomes Provided for Goal C:  
Develop New or Improved Approaches for Preventing or Delaying  
the Onset or Progression of Disease and Disability**

**SCIENCE ADVANCES**

- Oxygen Restrictions and Retinopathy of Prematurity
- HIV Strains Responsible for Today's AIDS Epidemic Dated to Early 20th Century
- Vaccine Candidates for Plasmodium falciparum and Plasmodium vivax Obstruct Parasite Invasion of Red Blood Cells
- The Effects of El Nino on Severe Diarrheal Diseases in Peruvian Children
- Mapping Heroin Trafficking Routes Predict HIV Transmission
- Mother-to-child Transmission of HIV Infection Through Breast Feeding
- Protein Found During Pregnancy Predicts Preterm Birth

**SCIENCE CAPSULES**

- Ignition-Lock Device Prevents Drunk Driving
- Male-Female Differences in Drug Use Traced to Differences in Opportunity to Use
- Seniors' CAM Habits Reinforce Necessity of Physician-Patient Dialogue
- CAM Use in Cancer Patients
- Video Series Helps Parents Improve Infant Health
- Researchers Find Important Protective Immune Differences in HIV-Infected and Uninfected Women
- Relationship With Mothers Influences Teen Sexual Behavior
- HIV Infection Does Not Increase Complications From Cesarean Delivery
- Exposure to Allergens During Infancy May Prevent a Lifetime of Allergic Asthma
- Infection Rates Decrease Among U.S. Blood Donors
- Researchers Identify a Potential Therapeutic Compound for Reducing Stroke Damage
- Hostility may be Associated with Early Atherosclerosis
- Reducing Children's Television Viewing May Prevent Obesity
- Older (and Cheaper) Blood Pressure Drug Holds its Own
- Risk of Antibiotic Treatment of E. coli O157:H7 Infection
- Walking Reduces Risk of Type 2 Diabetes in Women
- Predictors of Smoking Cessation in Adolescents
- New Guidelines for Treating Tobacco Use and Dependence
- Lack of Effect of Dietary Fiber on Recurrence of Colorectal Adenomas
- Breast Cancer Risk after Surgical Removal of the Ovaries in BRCA1 Mutation Carriers
- Weighing the Risks and Benefits of Tamoxifen Treatment for Preventing Breast Cancer
- Updated Atlas of Cancer Mortality Released
- Update on Efforts to Develop a Vaccine for Otitis Media
- First Fractures in Older Women and Men Should Not Be Ignored
- Simplified Screening Test for Hyperlipidemia
- Treatment Can Reduce Negative Effects of Maternal Depression on Children's Cognitive Development
- Newer Medications are Helping Patients with Schizophrenia Reduce their Abuse of Drugs and Alcohol
- Psychopathology Overlooked as Factor in Spouse Abuse
- Nurse Home Visitation Carries Beneficial Effects for African American Mothers Too

**Titles of NIH Research Outcomes Provided for Goal C:  
Develop New or Improved Approaches for Preventing or Delaying  
the Onset or Progression of Disease and Disability**

**SCIENCE CAPSULES**

- Neuropsychological Functioning Associated with CSF HIV in Patients Receiving Anti-Retroviral Therapy
- Markedly Elevated HIV, Hepatitis C Prevalence in Those with Serious Mental Illness
- New Insights into Prejudice Reduction
- Identification of Genetic Risk Factors that Affect Occurrence of Oral Cancers in African-Americans
- Osteoarthritis More Prevalent in Younger Groups of Middle-Aged African-American and Caucasian Women than Expected
- Exercise Stress Testing May Not Be Needed for Older Persons Beginning an Exercise Program
- Commonly Prescribed Diuretic Protects Against Osteoporosis
- Highly Reduced Protection Against Streptococcus Pneumoniae after Deletion of a Single Heavy Chain Gene in Mouse
- Exercise as a Fall Prevention Program for Elderly Individuals
- Cardiovascular Disease Risk Factors in Young Diabetics
- Health Choices of Postpartum Mothers
- Leptin's Role in Women's Weight Loss
- Smoking Cessation Reduces Risk of Cataract
- New Light on the Mechanism of Autoimmunity
- New Insights into Retinal Damage Triggered by Infection
- Autoimmunity and the Eye
- Microbicide Proved to be Safe and Tolerable in Four International Sites
- Risk of HIV Infection Associated with Sexually Transmitted Diseases
- HIV Levels in Female Genital Secretions Strongly Correlate with Levels in Plasma
- Estimating Absorption of Iron from Common Foods Eaten in China
- Diversity of HIV type 1 in Senegal
- Multivitamin Supplements to Pregnant Women Improves Birth Weight but do not Reduce Transmission of HIV Infection

**STORIES OF DISCOVERY**

- Heart Disease and History – A Good Cholesterol Story
- 1930's Mystery Solved with Modern Day Technologies: New Prevention Principle Unveiled
- Reducing Mother-to-Child HIV Transmission in Less Developed Countries
- Investing in the Community Can Improve Outcomes for Infants
- Amount of HIV in the Blood is the Main Predictor of Virus Transmission Among Heterosexuals
- Novel Approaches to Vaccination Could Broaden Efficacy, Spare the Needle, and be Easier to Store and Administer

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

**Performance Targets & Results**

**Annual Target**

**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.**

*FY 2001-2002 performance to be reported in February 2002 and 2003, respectively.*

**FY 2000**

*Performance: Target substantially exceeded. 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.*

**FY 1999**

*Performance: Target substantially exceeded. 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.*

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

### ***Goal Background***

Early diagnosis and detection of disease is often a key requisite for effective treatment and prevention of disease and disability. Some of the most life-threatening diseases and disabilities can only be controlled or cured if they are diagnosed and treated in the earliest stages. Diagnostic methods include a broad array of biomedical technology, e.g., machines or instruments that directly visualize the body, tissues, or cells; instruments that can measure specific body functions; and tests that detect minute quantities of biological and inorganic materials. Regardless of their nature, diagnostic tools must be accurate and safe. It is also advantageous if they are inexpensive, noninvasive, easy to use and pain-free.

In the past, “diagnosis” meant the characterization or identification of a current disease or disability for the purpose of treatment. However, the realm of diagnosis has expanded in parallel with advances in basic disease research. Within the last few years, and intensified by the completion of the human genome project, a focus of the field of diagnosis has shifted to genetic testing. Scientists have now identified mutations in individual genes that can be used to confirm a diagnosis of ongoing disease, or even predict the development of disease in the future. Because genetic testing can be used to predict an individual’s risk of developing a particular disease, prevention, rather than treatment, has become a major aim of diagnostic measures. The accuracy and reliability of diagnostic tools based on genetic testing is particularly critical, because patients may make decisions about preventive measures or interventions in the absence of ongoing disease.

### ***Performance Assessment Approach***

#### *Basis and Data:*

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

The Working Group developed its assessment based on data provided by the ICs (science advances, science capsules, stories of discovery, and research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. (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 by the Working Group in assessing the outcomes of NIH research under Goal D in FY 2000 follow:

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 apply:

- ❑ 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 methods 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 are 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 to biological functions and behavior, or new findings are not published/and or disseminated.

*Validation and Verification:*

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.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

Target substantially exceeded. The Working Group unanimously concluded that the research outcomes submitted for FY 2000 assessment demonstrated that NIH had fulfilled the criteria (see *Performance Assessment Approach* above) for “substantially exceeding” Goal D.

The NIH Institutes and Centers submitted 50 science advances, science capsules, and stories of discovery (tabulated at the end of this section) that, in their judgment, demonstrated progress in the development of new or improved methods for diagnosing disease and disability.

### **Research Outcomes and Their Significance**

The Working Group noted the value of a variety of diagnostic methods, including instruments, immunological tests, and biochemical assays, to the prevention and treatment of disease and disability. Part of their discussion focused on the fact that gene discovery has had a significant impact on diagnosing disease, and this is underscored by the research studies the Working Group decided to highlight for purposes of this assessment. Of the 21 studies highlighted by the Working Group, only eight were *not* gene related. The assumption behind genetic diagnoses is

that research will uncover how mutations cause disease and will ultimately contribute to improvements in patient diagnosis, as well more accurate clinical screening, better genetic counseling, and highly effective preventive measures as well as therapeutics.

The Working Group categorized the advances it highlighted as having either immediate clinical applicability or the promise of future clinical value. Each of the studies reviewed exhibited potential to contribute to new and improved diagnostics. Some of the studies described new diagnostic assays that open possibilities for better detection or more accurate predictions. Several studies capitalized on technology to develop less invasive and painful methods of diagnosis. Additionally, the Working Group especially emphasized the innovative use of current tools.

### Of Immediate Diagnostic Value

The Working Group collectively agreed that several advances describing newly developed diagnostic tests and one advance re-evaluating the usefulness of a currently used diagnostic test were particularly noteworthy. Besides improving diagnosis, these advances reflect improved understanding of the causes of these diseases, and provide a basis for prevention and treatment.

*Tests for Infectious Disease.* The Working Group applauded the development by an international collaboration of a rapid method for diagnosing tuberculosis that takes only nine days rather than the three to four week necessary for traditional methods. In addition, the test can be used to determine whether an individual's bacteria are resistant to antibiotics that could be used for treatment. This rapid, inexpensive, and sensitive method should improve the capability to detect and properly treat tuberculosis in developing country health facilities.

The Group also highlighted the development of a new blood test for Lyme disease, which has been difficult to diagnose. Lyme disease is caused by the bacterium *Borrelia burgdorferi*, which is transmitted to people by infected ticks. The new test detects an immune response to a specific region of a protein produced by the bacterium, and is therefore very accurate. The test is capable of distinguishing individuals who have Lyme disease from those who exhibit an immune response because they have been vaccinated for Lyme disease. The test will therefore reliably identify individuals who require treatment, especially in the early-stages of Lyme disease when antibiotic treatment is most effective.

Another new test developed by NIH-funded scientists will be useful in the management of AIDS patients who are doing poorly on combination antiretroviral therapy because of the development of viral resistance to one or more of the antiretroviral drugs. The test screens for HIV mutations correlated with resistance to specific antiretroviral drugs. By identifying patients infected with strains of HIV that are likely to develop drug resistance, the test offers an opportunity to adjust their treatment regimens so as to retard drug resistance.

*Tests for Cancer.* The Working Group commented on the value of a study that characterized a population of older men who have a very low risk of developing prostate cancer. These men, aged 60-65, had very low concentrations of prostate specific antigen (PSA). Although screening for prostate cancer generally involves repeated testing for high concentrations of PSA until age



75 (after age 75, surgical treatment is usually unnecessary), repeated testing of these men with low initial values of PSA did not help detect this cancer. The elimination of screening in this low risk group could markedly reduce health care costs as well as ensure that testing and diagnosis is focused on those most at risk.

The Working Group also commented on a study that could lead to the development of an inexpensive, saliva-based test for breast cancer. NIH-funded researchers found that a protein found in malignant (but not benign) breast cancer tumors, is also found in serum and saliva. A simple salivary test used in combination with mammography and physical examination could improve cancer diagnosis.

Finally, the Working Group lauded several NIH-funded studies that concluded that a particular protein that regulates normal cell death (apoptosis) may be important in the development of cancer. In cancerous tissue, the gene that codes for the protein is improperly regulated, and an excessive amount of the protein (called survivin) is produced. Because of the high concentration of survivin, cells that would ordinarily die may proliferate, causing the tumor to grow. Thus, survivin holds promise both as a marker of cancer progression and as a possible target for therapeutic intervention. If researchers can block the production of survivin, they may be able to develop a successful cancer therapy.

#### Diagnostic Tests Based on Genetic Markers

Additional studies with immediate diagnostic value relied on gene discovery. These tests may be used to predict future diseases and disorders before they develop, or to identify individuals at risk for various diseases. Such early identification might help delay or prevent onset of disease.

The Working Group noted the diagnostic potential of an NIH-supported study of the genetic basis of lipodystrophy, a condition in which patients have defective fat metabolism and often, type 2 diabetes. Previous studies localized the gene that causes lipodystrophy to chromosome 1, and showed that this gene codes for a protein called lamin A/C, a component of the nuclear envelope. In the new study, researchers studying 14 families with lipodystrophy pinpointed four specific mutations in the gene, paving the way to a diagnostic test. Other researchers built on this knowledge by generating a mouse model of the disease, which may lead to better understanding, and perhaps treatment, of both lipodystrophy and type 2 diabetes. This study was one of a number of noteworthy investigations of the genetic basis of type 2 diabetes, which is a complex disease stemming from mutations of more than one gene, as well as other factors. However, NIH-funded research has identified several genes that contribute to susceptibility to this disease, suggesting productive leads for the development of future diagnostic methods and treatments.

Another NIH-funded study identified the genetic basis for a relatively rare but severe disease, pseudoxanthoma elasticum (PXE). PXE causes deterioration of the arteries and skin. Deterioration of blood vessels may necessitate bypass surgery in patients still in their twenties, and deterioration of the skin gives the appearance of premature aging. Ruptured vessels in the retina may lead to blindness, while rupture of those in the gastrointestinal tract may cause death. The researchers found that PXE is caused by mutations in a gene on chromosome 16 that codes

for a transport protein. This finding will make it possible to screen for this disorder and implement dietary interventions to lessen its impact.

NIH-funded scientists also determined the genetic basis for two congenital conditions stemming from malformations in a layer of cells called the ectoderm. The first study examined the basis for cleft lip/palate, a common birth defect which in some cases involves defects of the skin, teeth, and hands, and also mental retardation. The researchers found that mutations in a gene that codes for a cell-cell adhesion protein cause the syndrome. This finding will not only facilitate screening for the syndrome, but also improve our understanding of the processes involved in orofacial development. The second study examined the basis for a disorder called hypohidrotic ectodermal dysplasia, which affects the formation of teeth, hair, and sweat glands. Scientists found that mutations in a specific gene on chromosome 2 lead to the disorder. This finding not only provides a basis for diagnosis, but also for the development of therapies.

The Working Group highlighted the identification of a genetic basis for familial primary pulmonary hypertension (FPPH), a rare but devastating disorder in which structural changes in the blood vessels of the lung impede blood flow, overworking the heart and sometimes leading to heart failure and death. Scientists determined that defects in a gene coding for a cell surface receptor with an important role in lung development are found only in people who have this syndrome. In addition, defects in the gene may be related to a non-inherited form of this disorder. Thus, the discovery is likely to lead to new approaches for patient diagnosis and screening.

Within this theme of inherited disorders, the Working Group commented on the value of recent studies that identified four genetic defects leading to diseases of the kidney. In all four studies the mutated genes code for proteins associated with cellular structures in the kidney responsible for the normal filtration of fluid from the blood. Thus, the mutations cause defects in the filtration process, resulting in leakage of protein in the urine and kidney disease and failure. Studies of these proteins revolutionized the fundamental knowledge of the molecular mechanisms of filtration and will engender new strategies for diagnosis, treatment, and prevention of kidney diseases.

NIH-supported scientists also identified the genetic basis for an inherited sensory defect called Usher syndrome, which is the most common cause of blindness and deafness in Americans. The scientists found that mutations in a gene that encodes a protein called harmonin lead to one form of the syndrome prevalent among descendants of French settlers in Louisiana. Harmonin is expressed in sensory cells in the inner ear that are essential for hearing. Detection of mutations in the harmonin gene will permit diagnosis of both the retinal and auditory degeneration characteristic of Usher syndrome. In addition, the discovery of the genetic basis for this disease will improve our understanding of the molecular mechanisms underlying audition and vision.

#### Of Promising/Pre-Clinical Diagnostic Value

A number of studies discussed by the Working Group involve the development of new or improved diagnostic tools or methods that have great promise for future clinical application.

Although these advances are not immediately applicable to clinical situations, the Group believed that they will significantly improve health care and the quality of life in the future.

*Imaging Techniques.* Several studies highlighted by the Working Group involved the development of new or refined methods for the diagnosis of Alzheimer's disease. Often researchers are uncertain about the diagnosis of Alzheimer's disease as other forms of dementia (decrease in cognitive abilities) may sometimes mimic Alzheimer's. One such study developed a highly accurate method for predicting Alzheimer's disease using a powerful, currently available technology, magnetic resonance imaging. The investigators improved the accuracy of this technique by using it to analyze certain areas of the brain known to be involved at an early stage in the disease. Using this approach, the researchers were not only able to diagnose current disease status, but also to distinguish with high accuracy individuals who had memory impairments and later developed Alzheimer's from those who did not. Thus, the technique may be useful for identifying individuals at risk who would benefit from early treatment. Another study indicated that a different type of brain imaging, positron emission tomography, may be useful in the prediction of Alzheimer's disease in individuals genetically at risk. This study showed that individuals with a particular genetic risk factor had significantly lower brain metabolism in certain areas of the brain. However, before the technique can be used for clinical diagnosis, follow up studies will be necessary to determine whether these individuals actually develop Alzheimer's. In another study, researchers developed a chemical probe that may be used in the future to detect the beta-amyloid plaques found in the brains of Alzheimer's patients. The probe selectively labeled beta-amyloid plaques in a mouse model of Alzheimer's disease, and has the potential to be used in conjunction with radiological imaging to detect plaques in living patients. Although the Working Group primarily focused on imaging techniques for identifying individuals at risk of developing Alzheimer's, it also mentioned a study that used an entirely different approach. In that study, the researchers developed refinements in a clinical interview to improve the accuracy of predicting whether a patient with a questionable diagnosis of Alzheimer's disease will actually develop the disease.

The Working Group was also very enthusiastic about another study that relied upon imaging technology. By literally shining a light through the brain, and coupling the laser with real-time computer analysis, researchers pinpointed brain regions with fluctuating oxygen levels. This noninvasive procedure can monitor changes in brain oxygen levels in adults and critically ill newborns. Such promising direct applications of state-of-the-art technology are an important advance in the field of diagnostics.

*Molecular Genetics.* The Working Group also emphasized the potential diagnostic value of a number of studies of gene discovery and expression. In one such study, researchers discovered that they could identify strains of hepatitis C virus (HCV) that are likely to cause chronic hepatitis by examining the mutation rates of two viral genes. In patients who developed chronic hepatitis the two genes exhibited high mutation rates. By contrast, in those patients who cleared the virus, the viral gene mutation rates were low. Presumably, the low mutation rates in these genes permitted an effective immune response to develop, while a high rate facilitated evasion of the virus by the immune system and development of chronic disease. Knowledge of these characteristics of HCV will allow for more accurate prediction of the clinical course of disease.

Finally, the Working Group noted that the clinical use of microarray technology, which permits the analysis of several thousand genes at a time, could result in a dramatic advance in diagnosis. Members of the Working Group pointed out an advance from the Goal A that described the use of microarray technology to distinguish metastatic melanoma cells from those that do not metastasize. Specifically, the researchers used the technique to identify a gene that caused noninvasive, poorly metastatic melanoma cells to become invasive and metastatic. This finding has great clinical and diagnostic relevance because cancer cells that metastasize spread throughout the body are responsible for most cancer deaths. In addition, microarray technology enabled another NIH group to characterize metastatic B lymphoma, and yet another group studied the genes characterizing breast cancers. These studies should have a great impact on cancer treatment as well as diagnosis.

**Titles of NIH Research Outcomes Provided for Goal D:  
Develop New or Improved Methods for Diagnosing Disease and Disability**

**SCIENCE ADVANCES**

- More Evidence that Methamphetamine Produces Long-term Damage to Human Brain Cells
- Abuse of Stimulants Increases the Risk of HIV-related Brain Damage
- Pinpointing Genes for Kidney Disease of Diabetes
- Cost-Effectiveness Studies of Kidney Dialysis and Transplantation
- Deciphering the Genetics of Type 2 Diabetes
- Mutations in Nuclear Protein Linked to Lipodystrophy
- Common Polymorphisms of the GJB2 (Connexin 26) Gene and Hereditary Deafness
- The Neurobiology of Depression and Suicide
- Evidence for a Genomic Region Containing a Schizophrenia Susceptibility Gene
- Utilization of Mitochondrial DNA Mutations for Cancer Detection Using Body Fluids
- Use of Structural Magnetic Resonance Imaging to Predict who will get Alzheimer's Disease
- Rapid Inexpensive Method for Detecting Tuberculosis in Patient Sputum Samples
- University of Hawaii Identifies First Gene Mutations in a Blood Vessel Disease
- New Role of Progesterone in Pregnancy Maintenance
- Variation in the HOXA1 Gene Linked to Autism
- Genetic Studies of a Chronic Condition
- Familial Primary Pulmonary Hypertension Gene Identified
- Identification of One of the Genes Whose Mutations Cause Usher Syndrome
- Gene for Cleft Lip and Palate/Ectodermal Dysplasia Syndrome is Identified
- Gene for Autosomal-Hypohidrotic Ectodermal Dysplasia is Identified
- Changes in a Viral Surface Protein Predict Outcome of Hepatitis C Infection

**SCIENCE CAPSULES**

- Beta-Endorphin Could Mark Genetic Risk for Alcoholism
- Highly Active Antiretroviral Therapy Reverses Brain Metabolite Abnormalities of HIV/AIDS
- NIH Researchers Improve Techniques for Interviewing Child Abuse Victims
- Type 2 Diabetes in Children, Adolescents and Young Adults
- Determinants of Recovery from Acute Hepatitis C
- Epidemiology and Mode of Spread of H. pylori Infection
- Virus Can Cause Kidney Inflammation
- Cause of Kidney Stones Mapped to Chromosome 1
- Control of Blood Glucose and Blood Pressure Levels Reduces Diabetes-Related Complications
- Rapid Screening for Cystic Fibrosis Mutations in Nonhuman Primates
- Early Warning of Heart Trouble
- Shining a Light Through the Brain
- HPV DNA Testing in Cervical Cancer Screening
- Early Detection of Alzheimer's Disease
- Adult Consequences of Childhood Attention Deficit Hyperactivity Disorder are Common
- Measure of Sustained Attention Predicts Vulnerability to Future Schizophrenia Spectrum Conditions
- Tracing the Course of Prepubertal and Early Adolescent Bipolar Disorder

**Titles of NIH Research Outcomes Provided for Goal D:  
Develop New or Improved Methods for Diagnosing Disease and Disability**

**SCIENCE CAPSULES**

- Severe Eating Disorders Affect Black American Women
- Use of Saliva as a Source of Biomarkers for Cancer Diagnosis
- Standardized Clinical Information Can Predict Conversion to Alzheimer's Disease
- Pre-symptomatic Decline in Brain Function in Individuals at Genetic Risk for Alzheimer's Disease
- In Vivo Detection of Amyloid Plaques
- The Predictive Value of Low Prostate Specific Antigen (PSA) Levels in Older Men
- New Test Proves Useful for Management of AIDS
- New Test to Diagnose Lyme Disease
- Gene Linked to Developmental Syndrome in Old Order Amish
- Scientists Pinpoint Location of Possible Third Gene Involved in Hereditary Breast Cancer to Chromosome 13

**STORIES OF DISCOVERY**

- New Insights in Assessing the Safety of Insecticides
- Why the Kidney Sometimes Leaks Protein – Studies of Cells with Feet

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

### Performance Targets & Results

#### Annual Target

**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.**

*FY 2001-2002 performance to be reported in February 2002 and 2003, respectively.*

#### FY 2000

*Performance: Target substantially exceeded. 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.*

#### FY 1999

*Performance: Target substantially exceeded. 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.*

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

### ***Goal Background***

The aim of much NIH research is the development of new and improved therapeutics. This path to the goal of better health requires a strong foundation in understanding disease mechanisms and normal and abnormal biological functions. New therapeutics may involve the development of drugs, biologics, devices, or even changes in behavior. Thus, the search for therapeutics depends on advances in many areas, including structural biology, genetics, immunology, cellular and molecular biology, bioengineering, chemistry, enzymology, and pharmacology.

New and improved treatments for disease and disability range from the latest “high technology,” gene-based approaches, to “low technology” approaches that may be surprisingly cost effective yet significantly improve the quality of life. Thus, there are many different approaches for developing new therapies. For example, drug discovery may involve the rapid and accurate screening of thousands of biological extracts, or of vast libraries of structurally diverse molecules created through the use of combinatorial chemistry. However, NIH-funded efforts to develop new therapies often stem from advances in the understanding of basic biological pathways and mechanisms. Thus, knowledge of the molecular structures of physiologically important biological molecules has led to the development of drugs specifically tailored to fit specific biological targets such as receptors, enzymes, and hormones. In this way, drugs may be targeted to specific diseases or conditions. Gene-based and cell-based methods of treatment offer new approaches to treatment that may permanently correct a condition. Additionally, alternative and complementary medicines may provide low-cost approaches to treating diseases and symptoms. Finally, the development of behavioral interventions and the use of simple but effective treatments in the early phases of a disease may not only be cost effective, but may also result in lifelong improvements in the quality of life.

Clinical research is the final and essential pathway to the development of new therapeutics. New approaches—whether drugs, devices, or changes in behavior—ultimately must be evaluated in humans. Clinical trials of new interventions are vital to determining the safety and efficacy of any new therapeutic approach. NIH plays a central role in the development of new treatments by contributing to the generation of basic knowledge in support of clinical studies, and by developing therapies for diseases that might not be the focus of private sector efforts.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

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



The Working Group developed its assessment based on data provided by the ICs (science advances, science capsules, stories of discovery, and research awards/honors) that describes the new findings and theories forthcoming from the research that NIH conducts and supports. (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 by the Working Group in assessing the outcomes of NIH research under Goal E in FY 2000 follow:

The NIH biomedical research enterprise *has successfully met this goal* when its research yields new or improved approaches for treating disease and disability, 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 apply:

- 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 to biological functions and behavior, or new findings are not published/and or disseminated.

#### *Validation and Verification:*

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.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

Target substantially exceeded. The Working Group concluded that the research outcomes submitted for FY 2000 review demonstrated that NIH had been responsive to health needs, scientific opportunities, and development and utilization of new technologies and had fulfilled the criteria (see *Performance Assessment Approach* above) for “substantially exceeding” Goal E.

NIH's Institutes and Centers submitted 107 science advances, science capsules, and stories of discovery (tabulated at the end of this section) that, in their judgment, demonstrated progress in developing new or improved approaches for treating disease and disability. These outcomes represented a wide range of therapies, from medications, surgeries, and medical devices, to behavioral interventions and alternative approaches. They also reflected the various stages or steps involved in developing many therapies, from preclinical investigations—which often involve animal studies and cell and tissue studies—to progressive stages of human testing.

Based on the information reviewed by the Working Group, they found that NIH-funded research not only demonstrated the potential to lead to the development of new and improved treatments, but actually resulted in new and improved treatments that improved health care and the quality of life. Moreover, the individual advances discussed by the Working Group illustrate the fulfillment of other aspects of the criteria for substantially exceeding Goal E, such as the development of treatments that are more effective or have fewer side effects; relieve suffering; are less invasive or painful than current methods; and/or restore or increase physical function.

The Working Group noted further that each treatment advance represented the culmination of years, sometimes decades, of groundbreaking research, beginning most often with fundamental advances in the basic biomedical sciences. It is important to recognize that NIH research support of Goal A (Add to the Body of Knowledge about Normal and Abnormal Biological Functions and Behavior), forms the scientific base upon which academe, industry, and government develop new therapies. Thus, even though the Working Group concluded that the research outcomes provided to them demonstrates that NIH substantially exceeded Goal E, they 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 by NIH. Specifically, they noted that because outcomes for assessment are limited to those published in FY 2000, all progress for which NIH deserves credit is not captured. Moreover, Working Group members considered it likely that many of the drugs and devices approved by the FDA in FY 2000 were critically dependent on years of NIH-supported basic and translational research.

## **Research Outcomes and Their Significance**

The Working Group highlighted a number of noteworthy advances that, in their judgment particularly illustrated how NIH fulfilled the criteria for having substantially exceeded the goal. The discussion of these advances is organized according to the five major themes identified just above.

### Understanding Basic Biological Processes Critical to the Development of Therapies

The development of therapies is enhanced by an understanding of the normal biology of a system, plus an understanding of how that normal biology breaks down during the initiation and progression of a disease or disorder. With knowledge of the normal and disease states in hand, development of therapies is not limited to random screening of candidate compounds, but can be targeted to the specific molecular steps underlying the disease process. NIH-funded studies of

the basic biological mechanisms of disease frequently form the basis for drug development by the private sector, as well as by NIH.

The Working Group cited the detailed understanding of the role of  $\beta$ -amyloid protein in the development of Alzheimer's disease (AD) as an example of an advance critical to the development of therapies for AD. The buildup in the brain of dense deposits of  $\beta$ -amyloid is thought to be the primary cause of the neurological degeneration of late-onset AD, which causes as many as 4 million cases of dementia in the U.S. Understanding of the molecular mechanisms that lead to the abnormal buildup of  $\beta$ -amyloid plaques is therefore critical to the development of measures to prevent its deposition, as well as to remove deposits that have already formed. Researchers have discovered that injecting  $\beta$ -amyloid into mice or administering it nasally causes an immune reaction that stops plaques from developing, much like a vaccination. And the identification of the enzymatic processes leading to the deposition of  $\beta$ -amyloid provides the basis for the development of drugs to inhibit its production, an area being intensely pursued by industry. The Working Group noted that NIH is already building on the many promising animal studies in this area, and it anticipates the results in the next year or two of a number of human clinical trials of agents to prevent or treat AD. These important trials include testing of anti-inflammatory drugs, vitamins, estrogens, and *Ginkgo biloba*.

In the field of vision research, the Working Group discussed efforts focusing on *intraocular inflammatory disease*, or *uveitis*, a common ocular disorder that mainly affects children and young adults. It has been estimated to cause about 10 percent of the severe visual handicap in the United States and if untreated can rapidly lead to blindness. The present therapies for these uveitic disorders are drugs that suppress the immune response. While they can be very useful in this regard, there are significant side effects in terms of toxicity as well as suppression of beneficial immune responses to microorganisms. It has been found that a large number of intraocular inflammatory conditions appear not to be caused by an infectious agent but rather by an altered immune response of the body to itself. Animal models for these diseases have helped in understanding this abnormal immune response seen in patients and to evaluate candidate therapies. The goal of vision scientists has been to better understand the underlying mechanisms that lead to autoimmunity and ocular inflammation, so as to more specifically turn off only the harmful response, and try to do so with minimal or no side effects. An antibody dubbed HAT (for Humanized Anti-T-activated) and given the trade name Zenopax®, has been found to be effective in both preventing the development of the experimental uveitis and in treating the disorder once it appears.

Another advance identified by the Working Group could bring relief to people suffering from *inflammatory bowel diseases* (IBD), known as Crohn's disease and ulcerative colitis, which affect nearly one million Americans. Both forms of IBD are chronic illnesses that typically affect children and young adults and have a major impact on their health and quality of life. Traditional therapy for IBD has consisted of immunosuppressive and anti-inflammatory drugs, antibiotics, and drugs to relieve the pain, fever, and other overt symptoms of the disease. Unfortunately, about one third of patients do not respond to medical treatment, and in patients who do respond, remission is usually followed by relapse. Research is yielding new clues about the common final manifestation of IBD: chronic inflammation of the intestinal tract. Because of the limitations of current treatments, researchers seek a fuller understanding of IBD at the

molecular level, in the hope of identifying novel targets for new therapies. One approach has been to develop antibodies that inhibit the action of pro-inflammatory cytokines, which are molecules that stimulate the inflammatory response. Another approach has been to inhibit the expression of genes that encode such cytokines. However, researchers anticipate that improvements in treatment of IBD are likely to come from the identification of the genetic lesions that give rise to the disease. Genetic diagnosis should permit not only the early detection of individuals at risk, but also suggest new targets for drug development.

Bone loss and its effect on health, especially in seniors, is a growing problem. Thus, to facilitate the development of new drugs to treat *osteoporosis*, the Working Group heartily endorsed the long-term investment in studies of the underlying mechanisms of bone loss and bone remodeling, as well as the development of cellular and animal models to study these processes. It has been known for some time that bone cells are responsive to the female hormone estrogen, which acts to slow down the removal of calcium from bone. Unfortunately, estrogen, when taken alone, has been shown in some studies to slightly increase a women's risk of developing breast and endometrial cancer. Responding to this elevated risk, NIH-funded scientists developed selective estrogen receptor modulators (SERM) to maximize the beneficial effects of estrogen on bone while minimizing the adverse effects on other organs and tissues.

In an advance that provides a new treatment approach for individuals with sickle cell disease, NIH-supported researchers found that treatment with nitric oxide (NO) increases oxygen affinity of sickle cells. It has been proposed that NO may cause small blood vessels to dilate, which would allow easier passage of the sickle shaped cells through small vessels and into surrounding tissue. These results suggest that new treatment strategies should be considered that utilize nitric oxide transport to improve blood flow through small vessels and into tissue.

The Working Group noted that other research has confirmed that NO is central to many other biological functions. Poisonous in large quantities, it nonetheless is produced in tiny amounts throughout the body. In addition to relaxing blood vessels, scientists have found that the gas could help brain cells communicate with each other and with immune cells, killing disease-causing organisms, as well as assisting in the body's response to burns. From these basic discoveries, researchers are developing a number of treatments for high blood pressure, stroke, heart failure, complications of diabetes, and impotence. In the first conclusive trial of its kind, researchers from the NIH Neonatal Research Network have shown that using inhaled NO is an effective therapy for hypoxic respiratory failure in full-term infants who fail to respond to maximal conventional therapy, including 100 percent oxygen. Based on these studies, inhaled NO therapy for newborns suffering from hypoxic respiratory failure was approved by the Food and Drug Administration as an acceptable medical treatment.

The Working Group also mentioned an advance of note in another area of infectious diseases, the spongiform encephalopathies (TSE), which are degenerative, invariably fatal brain disorders in animals and humans. The most common TSE diseases are scrapie in sheep, bovine spongiform encephalopathy or "mad cow disease" in cattle, and Creutzfeldt-Jakob disease in humans. The infectious agent that causes TSE diseases, called a prion (for proteinaceous infectious agent) is associated with an aberrant form of a normal cellular protein, PrP. Researchers have discovered that a family of chemical compounds known as cyclic tetrapyrroles can significantly slow

disease progression in mice experimentally infected with scrapie. The cyclic tetrapyrroles appear to interfere with the conversion of the normal protein to an abnormal protein. By significantly impairing this transformation the cyclic tetrapyrroles delay the onset of disease.

In the field of mental illness, the Working Group cited the importance of new research focused on improved treatments. For example, lithium is the main pharmacological treatment for bipolar disorder. When taken regularly, it can effectively stabilize mania and depression in many patients and can reduce the likelihood that episodes of illness will recur. However, after more than three decades of use in the U.S., scientists still do not understand how lithium works, and why it works well for some people, but not others. Several NIH-supported projects have shown that lithium can positively affect the way nerve cells survive, change their shapes and metabolic rates, and form connections with other nerve cells. This unexpected action of lithium in maintaining and protecting the health of cells may have a significant impact on our understanding of its therapeutic mechanism of action. Researchers have now shown that lithium exerts protective and positive effects in the human brain. This evidence of lithium's neuroprotective properties at therapeutic concentrations provides the groundwork for larger, longitudinal studies to determine if lithium reduces or delays neuronal cell death and atrophy in patients with bipolar disorder. The Working Group considered this advance important because it could lead to the identification of new cellular and molecular targets of lithium's actions and will inform the development of new and better treatments for bipolar disorder.

Another class of medications used in treating mental disorders, called benzodiazepines (BZ), of which Valium® is a prototype, are usually very effective at reducing anxiety, but do not work in all patients. To understand why this might occur, scientists developed a model of anxiety by "knocking out," or deleting, a particular serotonin receptor in mice. These mice with the missing serotonin receptors displayed symptoms of anxious behavior, but did not respond to the relaxing effects of a BZ compound. This study identifies specifically which components of a brain transmitter system are likely to be involved in anxiety. The information affords basic scientists a specific therapeutic target for developing drugs to help BZ-insensitive individuals and, more immediately, provides clinicians a compelling rationale for prescribing currently available drug alternatives to BZ-insensitive individuals.

The Working Group noted an important advance that found a new use for an existing agent. Kaposi's sarcoma (KS), the most common cancer in patients infected with the human immunodeficiency virus (HIV), depends heavily on the development of tiny blood vessels (angiogenesis) to feed the tumors. In a recent study, KS patients were treated with thalidomide, a drug with known anti-angiogenic properties. Tumors shrunk in nearly half of the patients; it is likely that thalidomide caused the shrinkage through its anti-angiogenic activity. While additional studies are needed, this study, in addition to suggesting an effective new treatment for KS, is one of the first studies to demonstrate that an anti-angiogenic drug can cause remissions in an established tumor.

### New Approaches to Treatment

In addition to the established pharmacological approaches to drug development relying upon relatively small inorganic and organic molecules, a number of new approaches to treatment have

been developed that exploit the increasingly sophisticated ability to manipulate and deliver biologically-based therapies based on genes, cells, and enzymes. These approaches depend not only on a greater understanding of the genetics, cell biology, and enzymology of disease processes, but also on the use of recombinant DNA technology to transfer genes or provide essentially unlimited sources of pure proteins, and on advances in cell biology that permit the growth and differentiation of useful cell types in culture.

*Gene therapy.* The goal of gene therapy is to provide a patient with new genes to stop the progression of disease or even prevent it, or restore function, ideally on a permanent basis. This technically sophisticated approach is beginning to bear fruit. To avoid therapeutic misconceptions, it is frequently referred to as gene transfer, reflecting one of the field's greatest challenges—the need to develop safe and efficient ways to transfer genes to specific tissues in a patient's body.

For example, many viral-based vectors have shown potential as vehicles for gene delivery including: adenovirus, herpesvirus, retrovirus, and adeno-associated virus (AAV). However, there are some drawbacks in the use of viral vectors because the viral proteins can induce an immune response. In addition, a major shortcoming of AAV vectors is the size limitation of the genetic material that can be incorporated into the vector. Thus, diseases caused by defective genes with coding regions larger than 5,000 base part, such as Hemophilia A or Duchenne muscular dystrophy, cannot be treated using the AAV vector systems. NIH-supported researchers have demonstrated that recombinant AAV (rAAV) vectors can indeed be used to deliver therapeutic genes larger than 5,000 base part.

Another group of NIH-supported researchers is examining alternative approaches to the use of viral vectors for gene therapy. One method currently under study is the use of “naked DNA,” either alone or in conjunction with other materials. In the past decade, this approach has been successfully used *in vivo* and has produced transient gene expression in the liver, lung, muscle, skin, and heart. In related research, NIH researchers created a new hybrid vector by taking two pieces of a retrovirus (called MoMLV) and inserting them into an adenovirus. In cell culture and animal studies, the new hybrid was successfully integrated into the genome of a variety of cell types, both dividing and non-dividing. Additionally, the animal studies showed that the transferred genetic material could function for as long as three months.

Hemophilia B has been the focus of recent gene transfer research. Current treatment entails regular intravenous infusion of clotting factor to prevent the crippling joint damage and life-threatening bleeding complications of the disease. Although treatments have become safer, therapeutic products are still not risk-free; patients are at risk of contracting blood-borne diseases through their numerous transfusions. The ultimate goal is to offer a cure for the disease, and one hope for a cure comes from gene therapy. After promising preclinical studies in animal models, a gene therapy clinical trial was initiated in adults with hemophilia B. The gene was enclosed in a carrier vector, which was injected into the muscle of the patient. Results from the first three patients, who received the lowest dose of treatment, suggest that the vector may be safe and provides biologically active factor IX in the blood. Ongoing studies of these patients and of others will help to establish further safety parameters and therapeutic dosing for this gene therapy strategy.

Another candidate disease for gene therapy cited by the Working Group is Parkinson's disease. Several years ago scientists isolated a factor, called GDNF, that promotes survival and growth of neural cells, especially dopamine neurons. Short-term experiments in animal models of Parkinson's disease have reinforced the hope that GDNF might delay disease progression, but this goal has been thwarted by difficulties in providing sustained delivery of GDNF to appropriate cells within the human brain. Gene therapy is a potentially powerful method for delivering GDNF to the brain. Through genetic engineering technology, a team of scientists adapted a type of virus, called a lentivirus, to infect neural cells. In the future, this improved gene delivery system could prove useful slowing the progression of Parkinson's disease.

*Cell Therapy.* Cell-based therapy is based on the premise that whole cells can be coaxed to replace damaged or diseased cells, thereby repairing tissues and reducing the adverse effects of injuries and disease. Different types of cells may be used for this purpose, including embryonic and cells from particular tissues such as bone marrow. The Working Group highlighted a number of promising studies of the use of cell therapy for the treatment of various conditions, including spinal cord injury, liver failure, immunodeficiency, and inherited neurological disorders.

Embryonic stem cells are unspecialized cells in the early embryo that multiply and are capable of differentiating into all of the specialized cell types of the body. Because of this versatility, embryonic stem cell therapies have been proposed for many different nervous system disorders. For spinal cord injury, transplanted embryonic cells might give rise to new "nerve cells" that transmit signals between the brain and the body, or they might generate cells that support neurons. Such supportive cells might release substances that encourage regeneration of existing neurons or prevent them from dying; or they might provide a cellular form of insulation (myelin) essential to the electrical conduction of signals. The Working Group highlighted an advance demonstrating that transplanted embryonic stem cells survive, differentiate, and promote recovery in injured rat spinal cord. The researchers showed that neurons and supportive cells such as astrocytes and oligodendrocytes developed from transplanted embryonic stem cells treated with retinoic acid, a natural substance that promotes the differentiation of embryonic stem cells into neural tissue. In behavioral tests, the hind limbs of the treated rats regained some coordinated movement, although the animals could not walk normally. These results suggest that additional work in this area could lead to promising new treatments for people with spinal cord injuries.

The Working Group noted several advances in the area of bone marrow transplantation, including the use of bone marrow for the treatment of disorders of other tissues, as well as immune system disorders involving cells originating from bone marrow. For example, researchers tested whether bone marrow transplantation can be used to halt the progressive neurological deterioration in the childhood-onset form of X-linked adrenoleukodystrophy (X-ALD). X-ALD is a degenerative disorder of the central nervous system that leads to a vegetative state and death within 3-5 years. The researchers found that X-ALD patients who received bone marrow transplants at an early stage had no further decline in verbal or motor performance 5-10 years after treatment. Indeed, a few transplant recipients improved, or even had a complete reversal of symptoms. Scientists also documented the utility of bone marrow transplants for treating diseases of the liver. Although the liver may contain hepatic stem cells from which the

liver can regenerate, such cells have not been conclusively identified in adult human liver. Researchers who analyzed liver tissue obtained from women who had received a bone marrow transplant from a male donor found liver cells containing a Y chromosome. These findings demonstrate that mature, functional liver cells can be derived from circulating cells, most likely of bone marrow origin. Accordingly, the research has major implications for the management of fulminant hepatic failure and genetic liver diseases. Finally, the Working Group highlighted a study of the long term effectiveness of bone marrow transplants in maintaining the immune function of patients with severe combined immunodeficiency (SCID, or “bubble boy syndrome”). Although the thymus of SCID patients is underdeveloped, immune cells derived from the bone marrow transplant developed in the patients’ thymus glands, and continued to function for many years. These findings suggest that treatment of SCID with either bone marrow transplantation or gene therapy will produce long-lasting improvement.

Another area of transplantation research cited by the Working Group addressed the problem of rejection of transplants by the recipient’s immune system. This rejection is called graft-versus-host disease (GVHD), and is a serious problem for recipients of bone marrow transplants. Umbilical cord-blood is an alternative source of the blood-forming stem cells found in bone marrow. Thus, an international team of scientists compared the risk of developing GVHD from cord-blood and bone marrow transplants. They found that children who received a sibling’s cord-blood had a lower risk of GVHD than those who were treated with a sibling’s bone marrow. When combined with evidence that cord-blood donors need not match the recipients as closely as do bone marrow donors, this finding suggests that transplantation of cord-blood from unrelated donors may be useful for most children who need stem cell transplants, even those with hard-to-match tissue types.

*Enzyme Therapy.* In an advance characterized by the Working Group as superb, scientists developed an enzyme-based treatment for Fabry disease, the second most prevalent hereditary metabolic storage disease of humans. Symptoms of Fabry disease, which appear during childhood or adolescence, include severe pain in the extremities, skin lesions, and corneal abnormalities. With increasing age the disease affects vital organs, and death usually occurs during the fourth or fifth decade. Fabry disease is caused by insufficient activity of the enzyme  $\alpha$ -galactosidase A, which degrades a certain lipid (fatty substance). Thus, NIH-funded researchers used recombinant DNA technology to obtain an adequate supply of this enzyme for intravenous administration. In a phase I clinical trial, the researchers showed that  $\alpha$ -galactosidase A was safe, and that it reduced the concentration of the lipid in the liver, blood, and urine. A subsequent trial showed that the enzyme reduces pain in the extremities, and improves kidney and heart function. Thus, the researchers have applied to FDA for approval of  $\alpha$ -galactosidase A as a drug for the treatment of patients with Fabry disease.

#### Complementary and Alternative Approaches to Therapy

Complementary and alternative approaches to therapy encompass a wide variety of approaches, including herbal medicine, megavitamins, food supplements, acupuncture, traditional oriental medicine, folk remedies, and homeopathy. These therapies are often called holistic, meaning they consider the whole person. NIH-supported research in this area evaluates the safety and



efficacy of these products and practices, and examines possible interactions of these treatments with standard prescription or over-the-counter medications.

The Working Group emphasized the importance of a groundbreaking study showing that a widely used herbal remedy for depression, St. John's wort, decreases the effectiveness of indinavir, a prescription drug taken for the treatment of AIDS. Since depression is common in HIV-infected patients, they often take St. John's wort as well as drugs such as indinavir, a protease inhibitor. Herbal remedies are not regulated by the FDA, so little is known about possible interactions of these products with prescription medications. The NIH-funded researchers found that in healthy volunteers, St. John's wort decreased the concentration of indinavir in the blood by over 50 percent. The study has important clinical implications for HIV patients, because a large reduction in indinavir concentration could cause the development of antiretroviral resistance and treatment failure. More generally, the study is valuable because it heightens awareness of the possibility that herbal remedies, often thought to be safe because they are natural products, may interact with prescription drugs and decrease their effectiveness. The Working Group found this advance particularly noteworthy because the FDA subsequently issued a health advisory on St. John's wort drug interactions as a direct result of this study. Similar warnings were issued in Europe, and manufacturers of both St. John's wort and prescription drugs for HIV infection added this information to their product labels.

In another advance cited by the Working Group, scientists evaluated a natural extract of the Hemsley plant (*Cynanchum wilfordii*), for its potential in protecting the brain from the effects of aging. The Hemsley plant had originally been used as a diuretic in traditional Asian medical practice, but the scientists found that the extracted compound protected cultured nerve cells from harmful substances that accumulate in aging or diseased brains. These findings demonstrate that in addition to *Ginkgo biloba*, other botanicals may provide an important source of compounds worthy of study for their neuroprotective properties and possible use in treating dementia or memory loss.

The Working Group also noted research on the effectiveness of an ancient Chinese therapy, acupuncture, for the treatment of cocaine addiction. Currently, there are no approved medications for treatment of cocaine addiction. Patients either received auricular acupuncture, had a needle inserted at a location thought to be ineffective, or viewed a relaxation video. The researchers found that more than half of the acupuncture patients tested free of cocaine in the last week of treatment, compared to 24% of the control needle insertion group, and 9% of the relaxation group. The acupuncture patients also abstained from cocaine longer than the other participants. Thus, acupuncture in combination with other therapies may be an innovative, effective treatment for cocaine addiction.

#### Reducing the Costs and/or Improving the Quality of Treatment

The Working Group acknowledged the importance of NIH-supported efforts to improve the quality of life of patients through treatments that provide more efficient or effective approaches to care. Such advances may involve screening to detect the early signs of a condition while it is easily treatable, or "low technology" approaches that are surprisingly effective. Because treatments of this type often result in significant cost savings and do not have sufficient financial

payoff to attract the private sector, NIH has a unique role in supporting such research. Moreover, the Working Group noted that many treatments of this type, particularly when initiated at a young age, both increase lifetime productivity and decrease lifetime health care costs.

For example, NIH has supported the development of improved, low-cost treatment for people who have been severely burned. In many cases, the remaining skin is insufficient for skin grafts necessary to prevent infection and dangerous fluid loss. NIH-funded researchers cultured skin cells from burned patients and combined them with a polymer sheet to create living skin grafts in the laboratory. The Working Group noted that skin regeneration improved markedly with this technique, which is likely to decrease treatment costs and hospitalization times. NIH-funded researchers also developed techniques for managing the extreme pain that accompanies serious burns, particularly when bandages are changed. Researchers attempted to distract teenage burn patients during daily bandage changes by immersing them in a virtual reality environment that included an interactive glove and a helmet that projected 3-D images with a wide field of view, preventing the patients from seeing the procedure. The patients reported a dramatic drop in pain, anxiety, as well as focus on the procedure when immersed in virtual reality games. Virtual reality is a promising, low cost adjunct to pain medication that could make wound care less harrowing and improve overall healing for burn patients without the side effects of high doses of morphine-based drugs.

In another advance, researchers found that using smaller volumes of air as a ventilation strategy in treating acute respiratory distress syndrome (ARDS) could save an estimated 15,000 American lives each year, and could decrease health care costs by reducing the number of days on a ventilator in an intensive care unit. This new strategy for ventilator use reduced deaths by 22 percent compared with standard ventilation practices and also reduced the number of days spent on the ventilator. The new ventilator strategy was so successful in reducing deaths that the trial was halted early and all patients were then treated using the newer method.

Another study highlighted by the Working Group illustrates that a simple, inexpensive treatment—iron supplementation—could have a major impact on the academic achievements and behavioral development of children who are at risk. NIH-supported investigators compared adolescent children who were free of iron deficiency and growing normally, but had been treated for iron deficiency anemia as infants, with others who had not been iron deficient. Children who had severe, chronic iron deficiency in infancy scored lower on measures of mental and motor function, as well as attention, anxiety, and other social and behavioral problems. Because many African-American, Hispanic, and Mexican-American infants have iron deficiency anemia, this study highlights the importance of early screening for iron deficiency anemia, especially among minority infants who may be most at risk.

Another study found that the outcome of total hip and knee replacement is better when surgery is performed prior to advanced functional loss. Because of the risks of surgery, traditional practice has been to delay it until pain and functional limitation are intolerable. Although 90 percent of patients experience substantial relief from replacement surgery, the NIH-supported study showed that outcomes at 6 months postoperatively are worse for those who have advanced functional loss due to osteoarthritis of the hip or knee prior to the procedure. By affecting doctors'

recommendations about when to have surgery, this study may have a significant impact on the outcomes of the 270,000 hip and knee replacements performed annually in the United States.

### Treatment of Commercially Non-Viable Conditions

Sometimes when there is no clear financial interest in conducting research into new treatments, NIH becomes the major supporter of such research, particularly for research involving rare disorders or for conditions that are particularly stigmatizing, but nevertheless of substantial public health import. This support is critically important, noted the Working Group, and provides further evidence of NIH exceeding its goals in the area of treatment. For example, several advances have focused on new treatment options for addiction to heroin, cocaine, alcohol, and nicotine.

The Working Group noted one study that supports a more efficient treatment option for patients being treated for heroin addiction, by allowing physicians to give them a full month of methadone doses, rather than requiring them to attend a clinic at least once a week. Methadone maintenance therapy is known to be one of the most effective treatments available; in this study, only 12 out of 2,290 urine samples (0.5%) collected were positive for drugs. Methadone therapy not only reduces illicit opiate use, it reduces crime and the spread of infectious disease, and enhances social productivity. However, methadone therapy is only available to a small proportion of those who could benefit from it, perhaps as a result of legal requirements for weekly clinic visits. Reducing the frequency of clinic visits for stabilized methadone patients is not only more convenient for the patient, but also may allow clinics to concentrate more of their limited resources on less stable patients, and admit additional patients. Thus, the study may provide a rationale for changing the legal restrictions on prescribing methadone, and expand access to this valuable therapy.

Another study noted by the Working Group involved the development of a combination therapy for the treatment of individuals addicted to both heroin and cocaine. No medications have yet proven to be effective for the treatment of cocaine addiction. Although there are a number of effective treatments for heroin addiction, including methadone and buprenorphine, more than 50 percent of individuals addicted to heroin are also addicted to cocaine. An NIH-funded study examined the effectiveness of disulfiram (marketed as Antabuse®), a drug used for the treatment of alcoholism, on the cocaine dependence of patients who were also being treated for heroin addiction with buprenorphine. The researchers found that those who received this combination therapy abstained from cocaine use for longer periods of time than those who received only buprenorphine. Thus, disulfiram may be an effective treatment for cocaine addiction in heroin addicts who are being treated with buprenorphine.

The Working Group also recognized groundbreaking research by NIH-funded scientists in treating early-onset alcoholism, a severe form of alcoholism in which individuals become alcoholic before age 25. The scientists examined the effectiveness of ondansetron, a medication that blocks communications between certain neurons in the brain, for treating this disorder. Ondansetron was previously approved by the Food and Drug Administration for treatment of nausea in chemotherapy patients, and in a randomized trial, it significantly reduced alcohol consumption and increased abstinent days among patients with early-onset, but not late-onset,

alcoholism. Pending further studies, ondansetron might be indicated for early-onset alcoholism patients resistant to behavioral therapies alone.

The Working Group also highlighted emerging new treatments for nicotine addiction, which is at the root of one of the country's most serious public health problems, tobacco use. Research on nicotine addiction has led to a number of treatments including the nicotine patch, gum, and nasal spray, all of which help smokers alleviate the withdrawal symptoms that occur when they stop smoking. However, these treatments aren't always effective, so NIH-funded researchers developed a vaccine which has shown promise when tested in laboratory animals. The vaccine stimulates the immune system to produce antibodies that bind tightly to nicotine. The antibody-nicotine complex is too large to enter the brain, thereby preventing nicotine from producing its addictive effects. Another series of studies found that blocking the metabolism of nicotine with methsoxsalen, a drug originally used to treat skin disorders, can reduce smoking. By decreasing nicotine metabolism, methsoxsalen keeps blood levels of nicotine high, so that smokers need fewer cigarettes to replace the nicotine lost to metabolism. These studies pave the way for two new nicotine addiction treatments, thus offering a greater range of treatment options to individuals who want to quit smoking.

**Titles of NIH Research Outcomes Provided for Goal E:  
Develop New or Improved Approaches for Treating Disease and Disability**

**SCIENCE ADVANCES**

- Intellectual Impairment Does Not Affect Alcoholism Recovery
- Emerging New Treatments for Nicotine Addiction
- A Combination of Buprenorphine and Antabuse Appears Effective in Treating Individuals Addicted to Heroin and Cocaine
- New Behavioral Treatments for Marijuana Addiction
- Stabilized Methadone Patients Have New Treatment Options
- Clinical Toolbox Expands for Treating Heroin Addiction: Heroin Use Reduced by Medications
- New Hormones Show Promise as a Therapeutic and Male Contraceptive
- Long-Term Behavioral Effects of Iron Deficiency Anemia in Infancy
- Promising Target for New Drugs Against Malaria
- Severe Burn Patients During Bandage Changes
- Living Skin Grafts Enhance Burn Treatment
- Chemists Improve Synthesis of Anticancer Agent
- New Strategy to Prevent Lung and Liver Injury in Alpha 1-Antitrypsin Deficiency
- New Ventilation Strategy Saves Lives in Patients with Acute Respiratory Distress Syndrome
- Initial Results of Clinical Trial Raise Hopes for Gene Therapy
- Gene-Environment Interactions – A New Clue with Implications for Asthma
- Overcoming Obstacles to Islet Transplantation for Type 1 Diabetes
- Novel Approaches in Gene Transfer Delivery Methods
- Mutant Mice Offer Clues to Calcium Cycling in the Heart
- New Vector Enhances Gene Transfer
- Dopamine Receptor Agonists and Parkinson's Disease Treatment in Non-human Primate Models
- Experimental Technique Shows Promise in Treating Liver Metastases in Patients with Colorectal Cancer
- Novel Bone Marrow Transplant Procedure Offers New Hope to Patients with Cancers of the Blood
- Early Hormonal Therapy Extends Lives of Prostate Cancer Patients, Study Shows
- New Approaches to Bone Cancer Pain
- Progress in Enzyme Replacement Therapy for Fabry Disease
- Gene Therapy Strategy for Parkinson's Disease
- Embryonic Stem Cells Help Recovery from Spinal Cord Injury in Rats
- New Drug is Safe and Effective for Children and Teenagers with Juvenile Rheumatoid Arthritis
- Analysis Shows Glucosamine/Chondroitin Sulfate is Probably Useful for Osteoarthritis
- Osteoporosis Therapies Prevent Bone Cell Death
- Gene Therapy Restores Full Function in a Limb -Girdle Muscular Dystrophy
- Oxygen has a Positive Effect on Wound Healing
- Delaying Surgery to Replace Osteoarthritic Knees Results in Worse Functional Status
- Liposome-Mediated Gene Transfer Can Be Used to Treat Basal Cell Skin Cancer
- Bone-to-Bone Attachment May Be the Best Method for Reconstructive Hip Surgery
- Improved Treatment for Blood Clots in the Leg
- Widely Used Herbal Remedy, St. John's Wort, Found to Cause Significant Interaction with a Drug for the Treatment of HIV Infection

**Titles of NIH Research Outcomes Provided for Goal E:  
Develop New or Improved Approaches for Treating Disease and Disability**

**SCIENCE ADVANCES**

- The Role of HPA Axis Hyperactivity in Transducing Childhood Abuse into Adult Psychopathology
- New Insights into Lithium's Beneficial Effects in Bipolar Disorder
- Anti-anxiety Pills Don't Work For You? Maybe This is Why
- Translational Research Suggest Enhanced Treatment Strategy in Schizophrenia
- "Chili Pepper Receptor" A Target For Pain-Reducing Medications
- Treatment of Negative Symptoms in Schizophrenia
- Genomic Integration via a Hybrid Adeno-Retroviral Vector
- Scientists Find Potential Way to Improve Gene Therapy Delivery to Lungs and Brain
- Possible New Therapy for Leber's Congenital Amaurosis
- Cytomegalovirus Retinitis in AIDS Patients Treated with HAART
- Identification of a New Class of Compounds that Slows Development of a Prion Disease in Mice
- Therapies for Treating Infants with Severe Combined Immunodeficiency Show Long-lasting Benefits
- How Do Cancer Cells Resist Radiation Treatment?
- Viral Load Associated with Increased Risk of HIV Transmission
- HIV and Tuberculosis: Novel Approaches to Treatment
- Do "Epidurals" Prolong Labor and Increase Risk of Cesarean Delivery?

**SCIENCE CAPSULES**

- Anti-Nausea Medication Shows Promise in Treating a Severe Form of Alcoholism
- Treating Cocaine Addiction with an Ancient Chinese Therapy
- New Medications and Dosing Requirements Offer Options
- Medication Found Effective Against Toxic Effects of Cocaine in Mice
- Altering Brain Serotonin Levels May Reduce Aggressive and Impulsive Behaviors
- Better Understanding of Pain Mechanisms May Yield New Medications
- Testing with Magnets Speeds Recovery from Stroke or Brain Damage
- New Evidence Confirms Effect of Acupuncture on Morphine Withdrawal, Identifies Mechanism
- Natural Compound May Protect the Brain from the Effects of Aging
- Bone Marrow Transplant may have Long-Term Effect in Treating X-ALD
- Combination Therapy Improves Immune Function in HIV-1-Infected Children
- Development of New Anti-Cancer Agents
- Targeting the Body's HIV Sanctuary Sites
- New Class of Antibiotics
- Scaffolding for Nerve Cell Growth
- New Advice for Inhaled Corticosteroid Use in COPD
- Umbilical Cord Blood Transplants Continue to Show Promise for Pediatric Patients
- Cause of Kidney Failure in Diabetic Mice
- Nitric Oxide: Possible Treatment Approach for Sickle Cell Anemia
- Liver Cells Derived from Bone Marrow in Humans
- Correction of Membrane Lipid Imbalance Restores Phenotypic Expression in CFTR<sup>-/-</sup> Mice
- Improved Treatment for Cholera

**Titles of NIH Research Outcomes Provided for Goal E:  
Develop New or Improved Approaches for Treating Disease and Disability**

**SCIENCE CAPSULES**

- Genetic Correction of Sickle Cell Disease
- Agent Found Effective in Treating HIV Lipodystrophy Syndrome
- Successful Treatment of Kaposi's Sarcoma with Thalidomide
- Managing Menopausal Symptoms in Breast Cancer Survivors
- Progress with Antibodies as Anticancer Agents
- Treatment of Leukemia and Lymphoma with Recombinant Immunotoxins
- A New Approach for Treating Menstrual Epilepsy
- Drugs for Fabry Disease
- Minimizing "Secondary Damage" Following Spinal Cord Injury
- Tachyphylaxis May Not Exist!
- Interleukin-12 May Be Useful in Treatment of Cutaneous T-Cell Lymphoma
- Understanding the Immunologic Basis of Psoriasis Leads to Therapeutic Interventions
- Treatment for Lyme Disease Does Not Appear to Result in Long-Term Neurologic and Musculoskeletal Problems
- Endotoxins May Play a Role in Orthopaedic Implant Loosening
- Minimally-invasive, Image Guided, Percutaneous Tumor Ablation with Radiofrequency Energy
- Minimally-invasive, Image Guided, Percutaneous Tumor Ablation with Radiofrequency Energy
- New Imaging Technique for Following the Movements of Transplanted Brain Cells
- Improved Dental and Orthopedic Implants
- NSAIDs Suppress Alzheimer's Disease Pathology in an Animal Model
- Produce Produces Motor Benefits in Old Rats
- Gene Therapy with VEGF121 Gene Transfer Stimulates Angiogenesis for Treatment of Peripheral Muscle Ischemia in Rats
- The Impact of Hormone Replacement Therapy on Iron Status in Women
- New Less Toxic Immunosuppressive Drug
- New Drug to Aid in Protection Against Bioterrorism
- Promising Lead in Treatment of Hantavirus Pulmonary Syndrome
- The Many Faces of Nitric Oxide
- A New Approach to Dissecting the Cell Signaling Mechanism Involved in the Allergic Response

**STORIES OF DISCOVERY**

- Nitric Oxide: An Air Pollutant or Life Saving Treatment for Newborn Infants?
- Solving the Puzzle of Inflammatory Bowel Disease
- From Bench to Bone – Basic Research Yields Osteoporosis Treatments
- Interleukin-2 Receptor Targeting as Therapy for Sight-threatening Uveitic Disease
- Alzheimer's Disease Amyloid: Discovery of Molecular Processes Leads to New Therapeutic Approaches

**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.**

### Performance Targets & Results

#### FY 2002

##### Human Genome Project:

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.**
2. **Complete draft of the mouse genome (90% coverage, 99% accurate).**
3. **Obtain full-length clones and sequence data for 20,000 mammalian cDNAs.**

##### Genomes of Pathogenic Microbes:

4. **Establish a mechanism to facilitate access to resources, services, and technologies (bioinformatics, scanning, microarrays, genome chips) needed to investigate microbial gene function.**
5. **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).**
6. **Initiate pathogen genome sequencing projects for additional NIH priority areas based upon an updated Blue Ribbon Panel Report.**

*Performance to be reported in February 2003.*

#### FY 2001

##### Human Genome Project:

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).**
4. **Complete 2X depth of coverage toward the working draft of the mouse genome (90% coverage, 99% accurate).**
5. **Complete 1X depth of coverage toward the working draft of the rat genome (90% coverage, 99% accurate).**

##### Genomes of Pathogenic Microbes:

6. **Complete sequencing of five additional bacterial pathogens and five chromosomes of protozoan parasites.**
7. **Augment existing knowledge of pathogen genomes by initiating sequencing projects for at least six additional genomes (bacterial, fungal, parasitic).**



## Performance Targets & Results

### 8. Complete worldwide sequencing effort of the entire genome of *Plasmodium falciparum*.

*Performance to be reported in February 2002.*

#### FY 2000

##### Human Genome Project:

1. 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.

*Performance: Target met. The Human Genome Project public consortium reached a historic milestone in FY 2000 by completing a "working draft" of the sequence of the human genome (88% complete, 99.9% accurate). The U.S. contributed 67% of the working draft sequence; 87% of the U.S. total, by NIH.*

2. Finish the sequence of at least one human chromosome.

*Performance: Target significantly exceeded. The Human Genome Project public consortium completed the "finished" (99.99% accurate) sequence of two human chromosomes – chromosome 21 and chromosome 22 – during FY 2000.*

3. Complete sequence of the genome of *Drosophila melanogaster* (excluding heterochromatin).

*Performance: Target met. During FY 2000, a consortium of publicly funded scientists, in collaboration with a private company (Celera Genomics), published the genome sequence of the fruit fly (*Drosophila melanogaster*).*

#### FY 1999

##### Human Genome Project:

1. Reach U.S. annual production rate of human genomic sequence of 90 million base-pairs.

*Performance: Target significantly exceeded. A U.S. production rate of 173 million base-pairs was achieved in FY 1999. (The corresponding FY 1998 rate was 50 million base-pairs.)*

2. Reach worldwide annual production rate of human genomic sequence of 220 million base-pairs.

*Performance: Target significantly exceeded. The world-wide production rate achieved in FY 1999 was 265 million base-pairs. (The world-wide rate in FY 1998 was 90 million base-pairs.)*

3. Total human genomic sequence completed worldwide at the end of FY 1999 at 400 million base-pairs.

*Performance: Target met. Completed sequence world-wide at the end of FY 1999 was 442 million base-pairs. This figure represents finished, high quality (an error rate of less than 1 in 10,000 base pairs) sequence data that is deposited and available to anyone in the U.S. public database, GenBank. (At the end of FY 1998, the total completed sequence was 180 million base-pairs.)*

<b>Performance Targets &amp; Results</b>
<p>4. Complete the sequence of the <i>C.elegans</i> genome (97 million base-pairs).</p> <p style="text-align: center;"><i>Performance: Target met. The complete sequence of the C. elegans genome was published on December 11, 1998 in Science 282:2012-2018, 1998. (In FY 1998, 90 million base-pairs of the genome had been sequenced.)</i></p>

**Goal Background**Human Genome Project

The Human Genome Project (HGP) was started in 1990 and has, from its beginning, enjoyed significant success. A major goal of the Human Genome Project is 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 new, more effective, and inexpensive ways to diagnosis, treat and prevent disease.

Many of the project's initial goals have been achieved, including building maps that locate (or identify) 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 fiscal year 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, in March 1999, an international consortium, with the U.S. taking the lead, launched the full-scale effort to sequence the human genome. 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. 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 year, the international consortium intends to publish its results of the working draft of the human genome in early 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 is also working to sequence the entire genomes of pathogenic microbes. 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 pathogen mutations contribute to virulence and drug resistance. Many medically important microbes are being sequenced including the bacteria that cause tuberculosis, gonorrhea, chlamydia, and cholera and the protozoan that causes malaria.

In order 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 fiscal year 2000, the NIH entered into an agreement with the Defense Advanced Research Project Agency for sequencing the genomes of pathogens of bioterrorist potential, including the anthrax bacillus. 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, ten bacterial pathogens and three chromosomes of parasitic protozoa already are completely sequenced, i.e. 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. Approximately two-dozen additional genome sequencing projects are ongoing.

*Status of Pathogen and Parasitic Protozoa Chromosome Sequencing Projects*

<b>Pathogen</b>	<b>Disease</b>	<b>Year Published</b>
<i>Chlamydia pneumoniae</i>	Respiratory disease	2000
<i>Chlamydia trachomatis</i>	Chlamydia	1998; 2000
<i>Haemophilus ducreyi</i>	Chancroid	Manuscript in preparation
<i>Leishmania major</i> Chromosome 1	Cutaneous leishmaniasis	1999
<i>Mycobacterium tuberculosis</i>	TB	Manuscript in preparation
<i>Plasmodium falciparum</i> Chromosome 2	Malaria	1998
<i>Escherichia coli</i> Strain 0157:H7	Food borne disease, hemorrhagic colitis	2001
<i>Streptococcus pyogenes</i>	Group A strep	Manuscript to be published Feb 2001
<i>Trypanosoma brucei</i> Chromosome 2	African Sleeping Sickness	Manuscript in preparation
<i>Treponema pallidum</i>	Syphilis	1998
<i>Ureaplasma urealyticum</i>	Nongonococcal urethritis	2000
<i>Vibrio cholerae</i>	Cholera	2000
<i>Neisseria gonorrhoeae</i>	Gonorrhea	Manuscript in preparation

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.

In May 1999, NIH convened a Blue Ribbon Panel on Microbial Genomics to gain advice on the agency’s future role in pathogen genome sequencing and functional genomics. The Panel concurred with an NIH proposed policy change to support large-scale genome sequencing activities through Cooperative Agreements to promote a more active agency role in determining which organisms will be sequenced, thereby avoiding duplication of effort and facilitating cooperation with other funding agencies.

The Panel also concurred with an NIH proposed list of priority organisms and suggested that emphasis first be placed on sequencing the following pathogens: *Aspergillus fumigatus* (a fungus that causes bronchopulmonary disease), *Cryptococcus neoformans* (a yeast-like fungus that causes a variety of infections including meningitis), *Cryptosporidium parvum* (a parasite that causes diarrhea that in immuno-compromised persons can be prolonged, severe, and even fatal), *Schistosoma mansoni* (a worm parasite that invades the wall of the large intestine and the liver causing inflammation and fibrosis), *Staphylococcus epidermidis* (a bacteria that causes various staph infections); as well as a number of oral pathogens including *Streptococcus gordonii*, *Fusobacterium nucleatum*, *Streptococcus mitis*, *Streptococcus sobrinus*, *Bacteroides forsythus*, and *Prevotella intermedia*, *Actinomyces* species. In addition, the panel emphasized the importance of sequencing the genome of *Anopheles gambiae* (the mosquito that carries malaria). Finally, the Blue Ribbon Panel recommended that NIH provide resources and infrastructure to enable investigators to gain access to emerging technologies for whole genome and organism approaches to functional genomics (e.g. relational databases, computational tools, microarrays, proteomics).

NIH is in the process of implementing its new policy for the support of large-scale genome projects and anticipates the release of an RFP to further the support of microbial genomics and post-genomics activities. In addition, a resource is being developed that will provide resources and databases for determining host immune responses to and individuals’ genetic susceptibility to microbial pathogens.

### ***Performance Assessment Approach***

#### *Basis and Data:*

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 sequences, BAC end sequences, and other sequence data, and progress in sequencing full-length human cDNAs. Publication will be the basis for documentation of the completion of the sequencing of additional pathogen genomes.

Performance assessment measures for initiation of sequencing projects and establishment of technologies and centers will include Program Announcements, Requests for Proposals, and other solicitations.

#### *Validation and Verification:*

Both finished and draft sequence data for human and mouse 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 Web site and publication.

Single nucleotide polymorphisms (SNPs) are deposited into a public database, dbSNP, and totals are reported on an NIH web site: <http://www.ncbi.nlm.nih.gov/SNP/index.html>. Sequence data for the full-length cDNA clones will be deposited into GenBank and identified as part of the Mammalian Gene Collection (<http://www.ncbi.nlm.nih.gov/MGC/>). Clones will be available to researchers from a central repository. Pathogen genome sequences are deposited in public databases (including GenBank) that have intranet sites and are published. Initiatives are announced in the *NIH Guide*.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

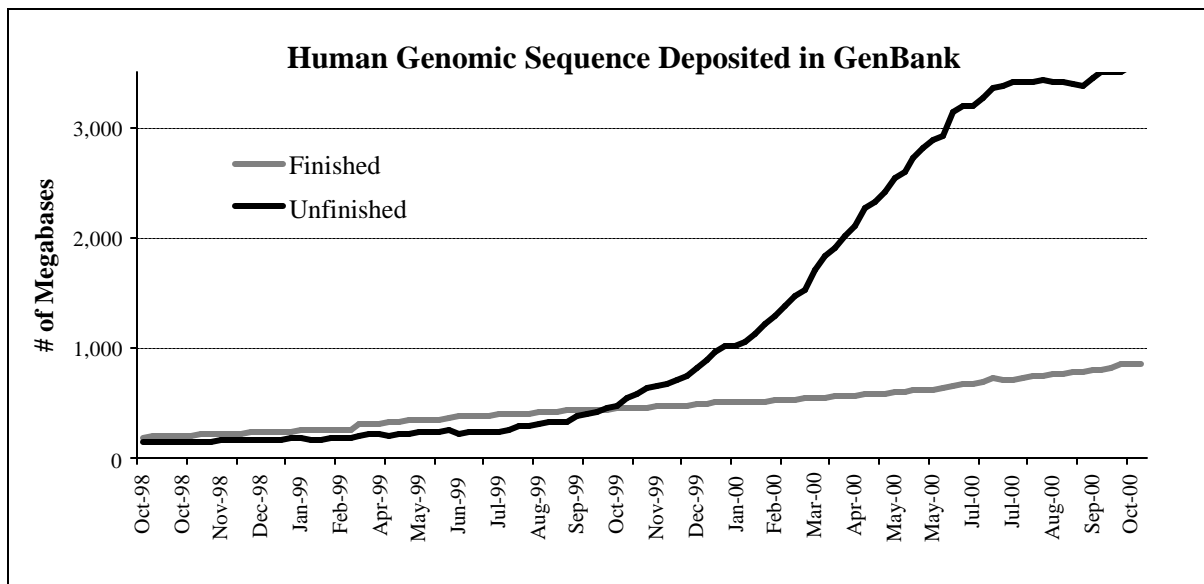
**Target 1: Worldwide effort completes "working draft" of human genome sequence (90% complete, 99% accurate). U.S. contributes two-thirds of that amount, and NIH contributes 85% of U.S. total.**

Target met. On June 26, 2000, the Human Genome Project public consortium made the historic announcement that it has assembled a working draft of the sequence of the human genome. This major milestone involved two tasks: placing large fragments of DNA in the proper order to cover all of the human chromosomes, and determining the DNA sequence of these fragments. With data updated through September 30, 2000, the assembly consists of overlapping fragments

covering 97 percent of the human genome, of which sequence has already been assembled for 88 percent of the genome. The average accuracy of all of the DNA sequence in this assembly is 99.9 percent.

Production of genome sequence had skyrocketed for the 15 months preceding the June 2000 announcement, with more than 60 percent of the sequence having been produced between January and June 2000 alone.

During this time, the consortium has been producing 1,000 bases a second of raw sequence -- 7 days a week, 24 hours a day. The average quality of the "working draft" sequence far exceeds the consortium's original expectations for this intermediate product. As a result, the "working draft" is substantially closer to the ultimate "finished" form than the consortium expected at this stage.



“Finished” sequence is 99.99% accurate and the only gaps that remain are from regions that are impossible to clone or sequence by current methods. All such gaps are identified and annotated in the database; the gap sizes are determined; and all of the efforts made to close them are recorded.

Approximately 50 percent of the genome sequence is in near- "finished" form or better, and 30 percent of it is in completely "finished" form. So while the percentage completed is slightly less than the target (88 vs. 90, respectively) the fact that the working draft is 10-fold more accurate than targeted, means that the Human Genome Project is further toward its ultimate goal of having the human genome sequence in finished form.

Assessment Data: Public funding of the Human Genome Project is predicated on the belief that public availability of the human sequence in the shortest possible time will lead to the greatest public good. All participants in the HGP have agreed to adhere to specific procedures, including

maintaining quality standards and making daily deposits of sequence information into the public databases. This information is maintained in the U.S. by the National Center for Biotechnology Information in the database GenBank

<http://www.ncbi.nlm.nih.gov/Genbank/GenbankOverview.html>. Scientists by the thousands, located worldwide, tap into GenBank every day to search for data to advance their medical research. The information in GenBank is available without restriction.

**Target 2: Finish the sequence of at least one human chromosome.**

Target significantly exceeded. The finished sequence for two entire human chromosomes (chromosomes 21 and 22) was completed in FY 2000. In the December 2, 1999 issue of *Nature*, an international team of researchers reported for the first time the sequencing of the 33.5 million base pairs of chromosome 22. The sequence included the longest, continuous stretch of DNA ever assembled, at over 23 million base pairs.

Just a few months later, scientists in Japan and Germany published, in the May 18, 2000 issue of *Nature*, the “finished” genetic sequence of human chromosome 21. Studying the organization of the genes on chromosome 21 and how they and their protein products function will help scientists find clues about Downs syndrome as well as other disorders, including Alzheimer disease, certain cancers, and manic depressive illness, which have also been linked to this chromosome. With the complete DNA sequence of chromosomes 22 and 21 now in hand, scientists can begin to study structural similarities between and among chromosomes as well as shared sequences.

Although “working draft” sequence allows for the recognition of most genes, the higher accuracy and completeness of “finished” sequence makes it a gold standard and remains the ultimate goal for human genome sequence.

Assessment Data:

Dunham, I., Shimizu, N., Roe, B.A., Chissoe *et al.*, “The DNA Sequence of Human Chromosome 22,” *Nature* 402:489-95, 1999.

The Chromosome 21 Mapping and Sequencing Consortium, “The DNA Sequence of Human Chromosome 21,” *Nature* 405:311-19, 2000.

**Target 3: Complete sequence of the genome of *Drosophila melanogaster* (excluding heterochromatin).**

Target met. In March 2000, a consortium of publicly funded scientists, in collaboration with a private company, Celera Genomics, published the genome sequence of the fruit fly (*Drosophila melanogaster*). The collaborators on the fruit fly genome project used different but very complementary strategies for sequencing the insect's genetic code, which consists of 165 million base pairs or chemical units.



The publicly funded groups contributed about 25 percent of the complete sequence in addition to very detailed genetic maps and a mapped scaffold of partial sequence. Celera contributed about 3 million random "whole genome shotgun" sequences and the computational expertise to assemble the results. The combined approach yielded the sequence of about 120 million base pairs of the fly genome including the portion of the genome containing the vast majority of genes.

The public and private groups also collaborated on the initial interpretation, or "annotation," of the fly sequence, identifying the location of the genes within the sequence. The public scientists will pursue refining and finishing the fly sequence. This effort primarily will involve closing the roughly 1,600 gaps remaining in the sequence.

#### Assessment Data:

Adams MD, Celniker SE, Holt RA, Evans CA, Gocayne JD, Amanatides PG, Scherer SE, *et al.* "The genome sequence of *Drosophila melanogaster*," *Science* 287:2185-95, 2000.

Myers EW, Sutton GG, Delcher AL, Dew IM, Fasulo DP, Flanigan MJ, Kravitz SA, *et al.*, "A whole-genome assembly of *Drosophila*," *Science* 287:2196-204, 2000.

### ***Progress Toward Goal Achievement***

This has been an historic year for the Human Genome Project. The production of a working draft of the human genome was a seminal achievement for biology and biomedical research. This achievement built on successful FY 1999 accomplishments in which 3 human genome sequencing goals were exceeded and a fourth goal was met, the complete genome sequencing the first animal, a roundworm. These successes have hastened the target date for completion of the final, high quality genome sequence to 2003 or earlier and have accelerated the plans for sequencing the genomes are two important mammalian model systems, the mouse and the rat.

### ***Next Steps***

The Human Genome Project will now focus on converting the "working draft" and near-"finished" sequences to a "finished" form. This will be done by filling the gaps in the "working draft" sequence and by increasing the overall sequence accuracy to 99.99 percent.

Although the "working draft" version is useful for most biomedical research, a highly accurate sequence that is as close to perfect as possible is critical for obtaining all the information there is to get from human sequence data. This has already been achieved for chromosomes 21 and 22, as well as for 30% of the entire genome.

**Goal g) Develop an AIDS vaccine by 2007.****Performance Targets & Results****FY 2001 and 2002**

1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.
2. Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.
3. Progress in collaborating with scientists in developing countries and with industry to further promote the development of vaccines for world-wide use
4. Progress in (a) completion of ongoing trials and (b) 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.

*Performance to be reported, respectively in February 2001 and February 2002.*

**FY 2000**

1. Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.

*Performance: Target met. Notable progress was made scientifically, as evidenced by safety and immunogenicity trials, and programmatically, through formation of the HIV Vaccine Trials Network and construction of the Vaccine Research Center.*

2. Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.

*Performance: Target met. A variety of existing animal models were utilized to make important advances in the development of vaccine candidates.*

3. Progress in collaborating with industry to enhance opportunities for vaccine development.

*Performance: Target met. The HIV Vaccine Design and Development Team awards made in FY 2000 substantially promote university-industry collaboration in the development of AIDS vaccines.*

4. Progress in (a) completion of ongoing trials and (b) 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.

*Performance: Target met. Three ongoing trials were completed and one new trial was initiated in FY 2000.*

## Performance Targets & Results

### FY 1999

1. Increases in the research portfolio supporting innovative vaccine discovery.

*Performance: Target met. The number and dollar value of awards made for vaccine discovery increased in FY 1999.*

2. Increased interactions between academic investigators and industry, to enhance opportunities for vaccine discovery and product development.

*Performance: Target met. A number of actions were taken to increase the interaction of academic investigators and industry.*

3. Progress in completion of ongoing trials and initiation of additional trials of new vaccine concepts and designs.

*Performance: Target met. Four new trials began and, of the seven clinical trials started in prior fiscal years, two more completed accrual.*

Note: In June 1997, the G-8 nations agreed to work to provide the resources necessary to accelerate AIDS vaccine research and to work together to enhance scientific cooperation and collaboration on development of a vaccine for AIDS. Building on this momentum, in his January 1997 State of the Union Address, former President Clinton announced the Millennium Vaccine Initiative, which calls for concerted international action to combat malaria, tuberculosis, and AIDS. At a meeting that March, leaders of pharmaceutical and biotechnology companies, international organizations, foundations, the public health community, and DHHS/NIH endorsed the Initiative.

### **Goal Background**

A safe and effective AIDS vaccine is a global public health imperative. AIDS is now the fourth leading cause of death and is the leading cause of disease burden in the developing world. An estimated 36 million people worldwide are living with HIV/AIDS. In sub-Saharan Africa, the worst affected area, there are countries where more than 20 percent of adults are infected. While the latest data show that the number of new cases of HIV in that area declined slightly between 1999 and 2000, the impact of the disease remains horrific.

HIV/AIDS will have 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 that AIDS is 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 U.S., the steep decline in HIV/AIDS deaths and in perinatally-acquired HIV/AIDS is an accomplishment of which the biomedical, pharmaceutical, medical, and public health communities can all be proud. However, the direct result of the decrease in HIV/AIDS deaths is that the number of people living with HIV/AIDS is increasing. Moreover, the fact that the number of new infections per year has remained at the same rate for almost a decade (about

40,000 per year) is of serious concern, as is the number of infections among people 13 to 24 years of age (14% of new infections annually).

There are many reasons to be optimistic that a useful HIV vaccine can be developed. Perhaps most compelling is the fact that the human immune system can control HIV under certain circumstances. Hope also comes from the results of animal testing and preliminary human trials. Experimental vaccines have shown some protection in animal models of AIDS. In Phase I and Phase II clinical trials, candidate HIV vaccines have been well tolerated and immunogenic. Moreover, candidate HIV vaccines have been observed to produce cellular immune responses active against a broad spectrum of HIV subtypes. These findings indicate that the problem of viral diversity may not be insurmountable. In addition, a basis for optimism comes from epidemiological studies that indicate that mucosal transmission is relatively inefficient in the absence of other sexually transmitted diseases. This suggests that moderate immune responses may prevent AIDS resulting from mucosal transmission of HIV. Finally, recent studies indicate that HIV vaccine efficacy trials among high-risk volunteers are feasible. Evidence of this feasibility means that considerable progress has been made in establishing the domestic and international infrastructure for the assessment of HIV vaccines.

Yet, many hurdles still must be overcome. A vaccine works by sensitizing the body's immune system to a particular disease-causing bacterium, virus, toxin, or a component of a pathogenic organism. When the infectious agent subsequently invades the body, the immune system recognizes it and mounts an immediate and robust response to destroy or contain the invader before it can cause disease. The many successes of traditional vaccines are well known, but other serious and fatal diseases still have proven stubbornly resistant to vaccines, demanding new approaches.

In 1997 the initiation of the Dale and Betty Bumpers Vaccine Research Center (VRC) was also announced. The VRC was created to conduct a comprehensive program of vaccine research on the NIH intramural campus. The VRC has succeeded in assembling a team of world renowned AIDS scientists and, late in the summer of 2000, these scientists began moving into their laboratories in the newly constructed VRC building and began working with scientists in academic, clinical, and industrial laboratories through a program of national and international collaborations. The primary focus of the VRC is to stimulate multi-disciplinary research, from basic and clinical immunology and virology through to vaccine design and production. The VRC will conceive, design, and prepare vaccine candidates for HIV and related viruses, and perform laboratory analysis, animal testing, and clinical trials on viable vaccine candidates.

Complementing the intramural NIH AIDS vaccine effort is an extensive extramural program. In all, 10 NIH units have activities to advance progress toward an AIDS vaccine. These activities include 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), considerable basic research relevant to vaccines on the part of the National Cancer Institute (NCI) and the National Heart Lung and Blood Institute (NHLBI), and a comprehensive Vaccine and Prevention Research Program conducted by the NIAID.

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.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

Narratives 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. NIAID databases and the NIH Guide 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.

#### ***Validation and Verification:***

Citations will be available for all science advances considered in the assessment process. NIAID databases, including SIMS (Scientific Information Management System), which is used to track initiatives, and the contract archives contain objective data on 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.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

#### **Target 1: Progress in the design and development of new or improved vaccine strategies and delivery/production technologies.**

Target met. Notable progress was made scientifically -- as evidenced by two human trials and several animal trials that have shown safety and ability to stimulate immune responses -- and programmatically -- through formation of the HIV Vaccine Trials Network and completion of construction of the VRC on the NIH campus.

To be globally effective, an HIV/AIDS vaccine will need to induce immune responses that are

broadly reactive (reactive to many different subtypes of HIV-1). Recently, NIH-supported investigators made a discovery that brings that goal closer to fulfillment. A recombinant HIV-1 protein, gp120, was known to induce high levels of antibodies; however, laboratory tests showed that those antibodies fight only certain subtypes of HIV-1. One theory explaining this narrow reactivity is that the gp120 protein being tested does not sufficiently resemble the gp120 protein complex as it occurs naturally on the surface of the HIV-1 virus. The native complex actually is composed of three gp120 molecules folded together, while the gp120 tested to date is a single molecule. Now, experiments by two NIH-supported research teams has shown how to increase the stability of the gp120 protein complex so that more native envelope-protein can be purified and tested as an immunogen. The hope is that the stabilized enveloped protein complex will be more potent and induce broadly reactive antibodies.

The HIV Network for Prevention Trials (HIVNET) recently completed its first international prevention vaccine trial. The trial, which took place in Uganda, evaluated an experimental vaccine based on a weakened canarypox virus that had been genetically altered to contain selected HIV genes. The tested vaccine proved safe and generated a broad-based HIV-specific immune response. Thus, there is hope that an HIV vaccine may help protect against exposure to various subtypes of HIV.

Intriguing new data suggest that vaccines designed to trigger an immune response to a small HIV protein called Tat could be a promising way to fend off the virus. "Killer" T cells targeted to the Tat protein can effectively contain Simian Immunodeficiency Virus (SIV), the monkey version of HIV. Four weeks after rhesus macaque monkeys were exposed to SIV, the Tat-specific killer T cells had eliminated the original subtype of SIV. The monkeys still had some SIV, but this SIV differed genetically from the original subtype. Current products in human vaccine trials primarily induce immune responses to envelope or other structural proteins of HIV rather than to functional proteins like Tat, which is required for the virus to replicate. If ongoing work shows that vaccinating monkeys with SIV Tat induces a massive killer T-cell response that can prevent infection or substantially reduce the amount of virus in monkeys, then research on HIV vaccines that incorporate similar targets will be stimulated.

Programmatically, perhaps the most important event in FY 2000 regarding development of HIV vaccines was the formation of the new international HIV Vaccine Trials Network (HVTN). The HVTN will provide a comprehensive, clinically based network to develop and test preventive HIV vaccines. In addition to the units based in the United States, participating sites will be located in sub-Saharan Africa, Asia, Latin America and the Caribbean. The network provides a coordinated, global framework in which to conduct clinical HIV vaccine research and thus will strengthen and expand NIH's HIV vaccine studies both domestically and in countries devastated by the AIDS pandemic. A Leadership Group coordinates the HVTN's clinical trials sites. The Leadership Group includes a Core Operations Center, which will provide administrative, technical and operational support, a Statistical and Data Management Center, and a Central Laboratory. NIH's HIV vaccine research program previously was centered in two separate groups (AVEG and HIVNET), one of which carried out early-stage testing of vaccine candidates, and the other which conducted trials of HIV vaccine and other prevention strategies. Building on the many accomplishments of the AVEG and HIVNET, the HVTN will conduct all

phases of clinical trials, from evaluating candidate vaccines for safety and the ability to stimulate immune responses, to testing vaccine efficacy.

In FY 2000, construction was completed on the new VRC building. This means that the VRC moves from being a virtual to a concrete center. The hiring of key center personnel has accelerated and as of August 2000 scientists began moving into the building and commencing their research.

Assessment Data: The science advances are documented in the following journal articles. Binley JM et al., *J. Virol.* 74 (2): 627-362, 2000. Yang X et al., *J. Virol.* 74 (10) : 4746-4754. H. Cao, et al. Preliminary data from this study was presented at the International Conference on AIDS in Durban, South Africa in July 2000 (Abstract LbOr24). Follow-up of this trial will continue for another 2 years. TM Allen et al. Tat-specific cytotoxic T lymphocytes select for SIV escape variants during resolution of primary viremia. *Nature* 407:386-90 (2000). BD Walker and PJR Goulder. Escape from the immune system. *Nature* 407:313-14 (2000). Journal articles and scientific meetings are the standard mechanisms for communication of scientific advances. *Virology* and *Nature* both are peer-reviewed journals. The International Conference on AIDS in Durban is the premier biennial event at which scientists involved in AIDS research share their latest findings. The HVTN program is documented in SIMS and the NIH Guide (RFAs: AI-99-009, AI-98-014).

## **Target 2: Progress in characterization, standardization, and utilization of animal models for evaluating candidate vaccines.**

Target met. Animal models continue to provide valuable information in advancing HIV vaccine research and in evaluating candidate vaccines.

Because HIV-1 does not infect monkeys, investigators have modified SIV, the immunodeficiency virus of monkeys, by exchanging the envelope, or outside coat of HIV-1 for the envelope of SIV. This virus, called SHIV, will infect monkeys. This makes it possible to evaluate the efficacy of HIV-1 envelope-based vaccines by immunizing monkeys with vaccines and then determining whether or not the monkeys can be infected with SHIV. Previously, SHIVs were made using the B subtype (clade) of HIV-1, the predominant subtype in North America. Now, investigators have made an SHIV using a clade C isolate of HIV-1 for use in animal testing of vaccines, topical microbicides, and other interventions to prevent transmission of HIV-1, subtype C. An animal model for this subtype is important because subtype C has become the dominant HIV-1 virus in the world, and vaccines for this subtype of HIV-1 will need to be tested in the primate model as they are being developed for use in Africa, China, and other regions of the world. This new virus has proved to be infectious in macaques.

In other studies, monkeys were used to determine which vaccine candidates and strategies best protect against SIV. The data indicated that an effective vaccine would need to stimulate both components of the immune system, namely neutralizing antibodies and cellular immune responses. These studies also showed that the most effective vaccination strategy is a

“prime/boost” regimen, in this case, vaccination with an immunogen created from the SIV envelope followed by vaccination with an immunogen created from the SIV core.

Animal models also are helping to move forward research involving DNA vaccines. DNA-based vaccines are a potential means to induce strong cellular immune responses and to prime for induction of antibody responses. To date however, this promise had not been realized because candidate DNA vaccines against HIV did not generate enough of the viral products (proteins) that cause an immune response and the resultant immune responses were weak. Now, NIH investigators have developed improved DNA vaccines that express more of the key viral products. The enhanced expression of these viral products has led to stronger immune responses during animal testing. Researchers have been able to induce strong immune responses in mice and to better contain SIV replication in the rhesus monkey model. The modifications to enhance expression of viral products now can be applied to development of DNA vaccines for testing in human clinical trials. In related studies, investigators used rhesus monkeys to test a “prime-boost” vaccination strategy. A DNA vaccine was used for the initial vaccination. The booster used a different vector, but expressed the same viral product as the prime vaccine. (Thus, a single antigen served as the immunogen in both the prime and boost vaccines.) This strategy induced a cellular immune response many times stronger than earlier tests with the DNA vaccine alone. The response was equivalent to what occurs during the initial phase of a natural infection.

Studies using macaques have shown that an antibody response alone can protect from infection transmitted through blood or mucous. Investigators derived particular antibodies from cells taken from HIV-infected humans and made identical copies. These monoclonal antibodies were injected into pregnant macaques and subsequently into their newborns. After delivery, the female macaques were challenged intravenously and the infants were challenged orally (mucosal exposure) with HIV different from that used to develop the monoclonal antibodies. Both the females and the infants were protected from infection.

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. The SVEUs provide NIH with a comprehensive means of vaccine evaluation by providing animals and vaccine efficacy assessment at the same site. NIH has solicited applications from facilities that can continue and expand the capabilities of the current SVEUs. The review of the applications has been completed and new awards will be made in FY 2001.

Assessment Data: The science advances are documented in the following journal articles: Chen Z et al., *J. Virol.* 74 (14): 6501-6510, 2000. Polacino PS et al., *J. Virol.*, 73(10): 8201-8215, 1999. Qui J-T et al., *J. Virol.* 73 (11): 9145-9152, 1999. Qui J-T et al., *J. Virol.* 74 (13): 5997-6005, 2000. Egan, MA et al., *J. Virol.* 74(16): 7485-7495, 2000. Allen TM et al., *J. Immunol.* 164: 4968-4978, 2000. Baba TW et al., *Nature Medicine*, 6(2): 200-210, 2000. The SVEU awards are documented in SIMS and in the electronic NIAID contracts archive as RFP-NIH-NIAID-DAIDS-01-04.

**Target 3: Progress in collaborating with industry to enhance opportunities for vaccine development.**



Target met. The HIV Vaccine Design and Development Team Awards made in FY 2000 substantially promote university and industry collaboration in the development of AIDS vaccines.

NIH launched four novel public-private partnerships to accelerate development of promising HIV/AIDS vaccines for use around the world. The new partnerships, called HIV Vaccine Design and Development Teams (HVDDTs), tap the different skills and talents of private industry and academic research centers, and provide incentive to move strong HIV/AIDS vaccine candidates out of the laboratory and into human testing. NIH has committed to spend approximately \$70 million over the next 5 years on the four HVDDT contracts that were awarded in FY 2000. The HVDDT program responds directly to the call to increase public-private cooperation in developing vaccines against globally important diseases such as AIDS, tuberculosis and malaria.

In addition, NIH initiated funding to advance the development efforts of two additional companies through other contract and grant mechanisms. In one case, NIH played a leadership role in bringing together scientists from the company and the International AIDS Vaccine Initiative (IAVI) to formulate and facilitate implementation of a cohesive development plan.

Moreover, on behalf of DHHS, NIH convened a major meeting on May 22-23, 2000, "Vaccines for HIV/AIDS, Malaria and Tuberculosis: Addressing the Presidential Challenge," to confront impediments to vaccine development in the private sector and to strengthen public-private partnerships for these vaccines.

Assessment Data: The HVDDT awards are documented in SIMS and in the electronic NIAID contracts archive as RFP-NIH-NIAID-DAIDS-00-10.

**Target 4: Progress in (a) completion of ongoing trials and (b) initiation of additional trials of new or improved concepts and designs, including the progression of promising candidates to larger trials testing vaccine candidates.**

Target met. Four ongoing trials were completed and one new trial was initiated in FY 2000.

In FY 2000, NIH completed four trials, progressed on six, and initiated one new trial. Although not initiated in FY00, substantial progress was made in preparation for the start of two new Phase-II vaccine trials, one domestic and the other in the Caribbean and Brazil, under the direction of the new HIV Vaccine Trials Network.

- A. As illustrated in Table 1, ten HIV vaccine clinical trials enrolling non-infected volunteers at the start of FY00 continued. During FY00, three of those trials were completed (protocol-specified follow-up concluded and participants entered a long-term follow-up protocol), and seven progressed toward completion.
- B. AVEG 038, a trial of Aventis Pasteur's ALVAC vCP205, began accrual in March 2000 and accomplished full accrual in May 2000; participants are continuing follow-up visits.

- C. In addition to these vaccine trials, volunteers who became infected after enrolling in a vaccine trial continue to be enrolled in and followed under one of the infected participant protocols, AVEG 402 or HIVNET 014A.

<b>Study</b>	<b>Vaccines Evaluated</b> (footnotes indicate sponsors of vaccine candidates)	<b>Accrual Initiated</b>	<b>Accrual Completed</b>	<b>Trial Status</b>
AVEG 027	ALVAC vCP205 <sup>1</sup> rgp120 MN <sup>2</sup>	11/97	10/98	Ongoing
AVEG 028	VVG203 <sup>3</sup> [attenuated S. Typhi- HIV-1 gp120]	12/97	5/99	Completed
AVEG 031	Gag-Pol DNA <sup>4</sup> Amended to add vCP205 <sup>1</sup>	11/98	2/99	Ongoing
AVEG 032	ALVAC vCP205 <sup>1</sup> +/- rgp120 SF-2 <sup>5</sup> , +/- p24 <sup>5</sup>	8/99	9/99	Ongoing
AVEG 033	ALVAC vCP205 <sup>1</sup> + GM-CS F <sup>6</sup> Amended to add Gag- Pol DNA <sup>4</sup>	1/98	6/98	Ongoing
AVEG 034	ALVAC vCP205 <sup>1</sup> or ALVAC vCP1452 <sup>1</sup> or ALVAC vCP1433 <sup>1</sup> ; +/- rgp160 MN/LAI-2	6/98	8/98	Completed
AVEG 034A	ALVAC vCP205 <sup>1</sup> or ALVAC vCP1452 <sup>1</sup>	9/99	12/99	Ongoing
AVEG 036	Rgp120 MN <sup>2</sup> or srgp120 MN or rgp120 MN/A244 (B/E) <sup>2</sup>	11/98	3/99	Completed
AVEG 202/ HIVNET 014	ALVAC vCP205 <sup>1</sup> +/- rgp120 SF-2 <sup>5</sup>	5/97	1/98	Ongoing
HIVNET 007	ALVAC vCP205 <sup>1</sup>	2/99	8/99	Ongoing

1. Aventis Pasteur; 2. VaxGen ; 3. University of Maryland; 4. Apollon/Wyeth Lederle; 5. Chiron; 6. Immunex

Assessment Data: The data on supported clinical trials come from the Statistical Center for HIV/AIDS Research and Prevention (SCHARP) at the Fred Hutchinson Cancer Research Center, Seattle, Washington.

### ***Progress Toward Goal Achievement***

Progress toward development of a vaccine for HIV/AIDS by 2007 is encouraging. Diverse approaches to HIV vaccine design are being pursued. Most initial work focused on the HIV envelope protein, which is the primary target for neutralizing antibodies in HIV-infected people. Significant advances and refinements in the envelope protein strategy have occurred and are being pursued, including use of different parts of the HIV-envelope (e.g., HIV surface protein

that is transiently exposed during binding and fusion with a target cell), stabilization of gp120, an HIV envelope protein complex, as well as other novel designs in early development.

As work with the HIV envelope protein advances, the pipeline of innovative concepts continues to generate new possibilities. Other strategies under investigation include DNA vaccines, candidate vaccines using functional proteins, e.g., Tat, in addition to structural proteins such as envelope proteins, combination vaccines, and vaccines that stimulate both components of the immune system (antibody and cell mediated responses). Each of these experimental approaches has proven efficacious to varying degrees in animal model tests.

Also, more vaccine candidates are reaching the human clinical trial stage. (Since 1987, more than 3,400 non-HIV-infected volunteers have enrolled in 54 NIH-supported preventive vaccine studies involving 28 vaccines. Of those studies, 52 were Phase-I safety studies and 2 were Phase-II safety and immunogenicity studies.)

Limited breadth of response to vaccine candidates and the lack of developed candidates for dominant subtypes continue to be serious hurdles. HIV is notoriously diverse in the number of subtypes circulating worldwide and a practical vaccine will need to protect against multiple subtypes. Nonetheless, progress is occurring. Last year, investigators identified a new immunogen for HIV, a normally hidden region of the HIV envelope. In test tube experiments, the immunogen neutralized 23 of 24 subtypes of HIV. Also, early testing of a combination vaccine demonstrated that the combination can stimulate both components of the immune system, antibody production and cellular immune response. This year, a Phase-I human clinical trial of a canarypox vaccine showed response to more than one subtype of HIV. Also, investigators stabilized gp120, an envelope protein complex. Scientists hope that this refinement will make the vaccine more potent and broadly reactive. Finally, research is addressing more HIV subtypes and the recent development of an animal model of subtype C, the dominant HIV-1 subtype, will enable investigators to more readily advance concepts based on that subtype to human trials.

The momentum for public-private partnership in HIV vaccine development has accelerated. This is a result of the May 2000 meeting “Addressing the Presidential Challenge” and the May 1999 workshop that brought together over 700 academic and industry investigators. In addition, the HIV Vaccine Design and Development Teams and the creation of the HVTN have increased the collaboration between government, academia and industry. The HVTN has formed several vaccine development teams, in partnership with DAIDS, to communicate and plan with companies the entry of products into clinical trials. Also, significant developments have occurred in the scientific and clinical research infrastructure for AIDS vaccine work with the establishment and building of the VRC and creation of HVTN.

### *Next Steps*

In FY 2002, NIH hopes to initiate an efficacy trial of a candidate HIV vaccine through the HVTN. This would be the first Phase III trial of an HIV vaccine candidate supported by the Federal government. In preparation for this important step, the HVTN held a two-day workshop,

in February 2000, to explore the complex issues posed by such a trial. In addition, the HVTN hopes to advance several new candidates into clinical trial by late FY2001 or early FY2002 and the VRC expects to initiate its first phase I clinical trial, a trial to assess safety of a DNA vaccine candidate.

While the next steps in working toward a vaccine for HIV/AIDS feature advancing vaccine candidates to later stages of clinical investigation, specifically evaluation of efficacy, it will be important to continue to initiate early clinical trials of new and improved candidates and to maintain a vigorous vaccine discovery and design effort so that the pipeline of potential candidates remains primed and the capacity to improve more advanced vaccine concepts is sustained. In FY 2001, several initiatives to encourage the development of HIV vaccines will be re-issued and expanded in order to ensure that those next steps are taken. These include:

- The Innovation Grant Program, which is designed to encourage novel ideas and approaches while stimulating interest from a new group of scientists, including those who had not been involved in HIV research previously.
- HIV Vaccine Research and Design, which supports basic vaccine research work including concept testing and the development of potential vaccine candidates.
- The Integrated Preclinical/Clinical AIDS Vaccine Development Program, which supports early clinical testing to establish the safety of vaccine candidates and basic laboratory work to understand and improve vaccine concepts that are in development.
- Laboratory Methods to Assess Responses to HIV Vaccine Candidates, a grant program to attract basic research to develop new, sensitive assays for the measurement of immune responses generated to candidate AIDS vaccines.

In addition, NIH plans include:

- Production of clinical grade DNA HIV candidate vaccines, at the VRC, in preparation for future phase I studies.
- Planning for a new vaccine manufacturing plant to be constructed on the NIH Frederick campus.
- Exploration of collaborative partnerships with pharmaceutical industry scientists regarding production of viral-vector vaccine candidates.

Also, plans are being formulated to engage the leadership of developing countries in formulating strategies and identifying additional research needed to help ensure rapid uptake of HIV vaccines, once available, in populations most in need.

In FY 2002, NIAID hopes to expand its HIV Vaccine Design and Development Teams initiative and the New Technologies for HIV and HIV Vaccine Related Research initiative. An important feature of the later initiative will be to facilitate application of new technologies, particularly new

chip technologies, to the development of assays. Also, NIH expects to launch the Comprehensive International Program of Research on AIDS (CIPRA), which, among other goals, will enhance the capacity of host countries to participate in the large-scale trials sponsored by the HVTN.

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### 2.1.2.2 Communication of Results

Communicating about health and science has long been recognized as a key NIH function. The Public Health Service Act of 1944, which defined the responsibilities of the Public Health Service (and the NIH) with respect to research, specifically authorized the PHS and NIH to "collect and make available through publications, and other appropriate means, information as to, and the practical applications of, such research and other activities." [Title III Sec. 301 (1)]

All of the NIH Institutes and Centers (ICs) conduct programs to collect, disseminate, and exchange information on medical and biological science, medicine, and health. The National Library of Medicine (NLM) is a Congressionally-mandated central resource for published biomedical information, which serves health care professionals, researchers, and the public worldwide.

The legislation that enables and directs the development of NIH programs has consistently emphasized the importance of informing the public about the results of health-related research. The authorizing legislation for all ICs includes "dissemination of health information" as an integral part of each Institute's basic mission. Information dissemination ensures that the science NIH conducts and supports is appropriately applied--whether by other scientists, health care providers, patients, or the public. Without the flow of information, the important results of research would languish at the researcher's bench.

Among NIH's most critical challenges in the realm of communicating research results are:

- Improving access to and use of NIH-based information within an increasingly competitive information environment.
- Ensuring access to appropriate health information among health care providers and facilitating the use of research-based innovation so that research advances translate into improved patient care.
- Ensuring access to appropriate health information among minority and other at-risk audiences.
- Increasing public and provider awareness, understanding, and willingness to participate in clinical research (clinical trials).

To meet these challenges, NIH works to improve outreach and access to health information. In some cases, NIH reaches out directly to health care providers and the public. In other cases, collaboration with organizations is initiated to increase attention to NIH-based information within the competitive information environment.

NIH is addressing access to information within a competitive information environment by working with organizations that have more direct access to providers (such as the American Academy of Family Physicians), using techniques such as telehealth technology and consolidated databases, and improving customer services. NIH also is addressing improvements in awareness of NIH-sponsored research among health care providers, in addition to developing

targeted campaigns and educational activities on significant health problems for patients and their families, and for minority, high risk, and low-access publics. Efforts also are under way to improve public and provider understanding of, access to, and support for clinical trials.



**Performance Goals Summary Table – Communication of Results**

Performance Goals	FY Targets	Actual Performance	Details
<p><b>a) Increase awareness of NIH-sponsored research among health care providers to promote research application.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Encourage the use of NINR-supported health care research findings in symptom management, health promotion, and disease prevention among health care practitioners.</li> <li>2. Communicate the results of research and collaborative activities that will accelerate the development of vaccines for emerging diseases and the application of vaccine strategies in less traditional areas (e.g., chronic diseases, autoimmune diseases, bioterrorism).</li> </ol> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. 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.</li> <li>2. 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.</li> <li>3. Increase awareness of NIDA-sponsored clinical treatment among health care providers.</li> <li>4. 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.</li> <li>5. Complete the expansion of 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</li> </ol>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p>	<p>Page 152</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>referrals for women, particularly those aged 65 and older.</p> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>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.</li> <li>2. Fund a series of demonstration projects applying telemedicine and other technology to improve the speed of reaching heart attack victims with lifesaving treatment.</li> <li>3. 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 Web site components that will allow users to interact on-line with live discussions, conferences, and other types of meetings.</li> <li>4. 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.</li> <li>5. Complete the evaluation of selected NIH outreach programs: a) 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, and b) the use of</li> </ol>	<p><b>FY 2000</b></p> <p>Target met. Model cases studies on 11 aspects of treatment for cardiovascular disease have been developed. Physicians who treat African-American patients have reached more that 600,000 other health professionals, patients, and members of the public with guidelines-based messages.</p> <p>Target met. Ten project awards were made.</p> <p>Target substantially met. Enhanced electronic outreach, on-line access to educational conferences, and a National Institute of Nursing Research listserv were all created.</p> <p>Target not met. Planning and preparation for the campaign to reach health professionals are still under way.</p> <p>Target met. a) The results of the evaluation are described in FY 2000 Target 1 above. b) Focus groups to evaluate whether physicians are using the guidelines were completed in Spring 2000.</p>	

Performance Goals	FY Targets	Actual Performance	Details
	<p>clinical practice guidelines on high blood pressure and obesity.</p> <p><b>FY 1999</b> 1. Evaluate several selected NIH outreach programs: a) 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, and b) the use of clinical practice guidelines on high blood pressure and obesity.</p>	<p><b>FY 1999</b> Target not met. a) Focus groups on physician practices in hypertension treatment with physicians, patients, and other and allied health professionals began in the summer of 1999. b) A practical guide and clinical guidelines on obesity are not yet complete. Use of these materials by physicians has not yet been examined.</p>	
<p><b>b) Increase awareness of NIH-sponsored research results among high risk, under-served, and/or affected publics.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Use NHLBI Enhanced Dissemination and Utilization Centers for asthma and cardiovascular disease to help decrease the excess mortality from these conditions in high risk communities.</li> <li>2. Increase awareness of the health implications of obesity to high risk, affected publics, such as African American women, and increase understanding about the health risks of overweight.</li> <li>3. Increase awareness of osteoporosis and related bone diseases in Hispanic and Asian individuals.</li> <li>4. Encourage prevention and management of chronic illnesses, e.g., diabetes and arthritis, among the nation's Hispanic populations.</li> <li>5. Develop and implement eye health awareness campaigns that target minority and underserved populations.</li> <li>6. Raise awareness of the benefits of vision rehabilitation among people over 65 and minority and underserved populations.</li> </ol> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Develop and implement an AIDS vaccine communication campaign to</li> </ol>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p>	<p>Page 160</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>increase awareness of AIDS vaccines before the initiation of a large efficacy trial.</p> <p>2. Increase understanding about the seriousness of diabetes and the importance of blood glucose control among African Americans, Asian/Pacific Islanders, and American Indians.</p> <p>3. Increase awareness of autoimmune diseases (such as rheumatoid arthritis, lupus, and scleroderma) among minority populations who are disproportionately affected.</p> <p>4. Increase awareness of sports injury prevention among parents.</p> <p>5. 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.</p> <p>6. Increase knowledge among Hispanic parents of the effects of drugs on the brain and encourage them to talk with their children about drug abuse.</p> <p>7. Increase awareness of the effects of drug abuse among Native American Indians.</p> <p><b>FY 2000</b></p> <p>1. Increase the available information on the benefits of exercise to older people.</p> <p>2. Develop and disseminate motivational messages related to breast and cervical screening to African American, Hispanic, and Asian communities.</p> <p>3. Expand programs on anxiety disorders and depression to audiences for whom language or literacy are challenges.</p>	<p><b>FY 2000</b></p> <p>Target met. Information about the benefit of exercise was made available through the news media, health fairs, and professional meetings.</p> <p>Target met. Motivational messages on these topics are being disseminated to these communities.</p> <p>Target met. A series of five easy to understand booklets on anxiety disorder have been developed. Similar materials</p>	

Performance Goals	FY Targets	Actual Performance	Details
	<p>4. Develop and disseminate easy-to-read and Spanish language health education materials on health issues to targeted special populations.</p> <p>5. Develop and implement diabetes awareness campaigns that target minority populations and their health care providers.</p> <p>6. 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.</p> <p>7. Pursue new outreach and collaboration initiatives to disseminate information and resources on rheumatic diseases in minority populations.</p> <p><b>FY 1999</b></p> <p>1. Develop and implement NIH information, education, and outreach programs on specific health issues: Breast Cancer and Mammography Education Program.</p> <p>2. Develop and implement NIH information, education, and outreach programs on specific health issues: extend the "Back to Sleep" campaign to target minority populations.</p> <p>3. Evaluate several selected NIH outreach programs: cardiovascular health outreach activities for Latinos.</p>	<p>for depression and bipolar disorder are under development.</p> <p>Target met. Several NIH Institutes developed and disseminated easy to read and Spanish language materials on various diseases and other health topics.</p> <p>Target met. Seven diabetes awareness campaigns targeting minority populations and seniors were developed and implemented.</p> <p>Target not met. The media summit was held, but not until December 2000.</p> <p>Target met. An African American Community Partnership has been launched.</p> <p><b>FY 1999</b></p> <p>Target met. NCI continued to implement the Breast Cancer and Mammography Education program.</p> <p>Target met. Major FY 99 accomplishments in the "Back to Sleep" campaign included an educational video, outreach to day care facilities, and creation of a coalition of African American organizations to promote back sleeping by infants.</p> <p>Target met. An evaluation of the community based outreach initiative "Salud para Su</p>	

Performance Goals	FY Targets	Actual Performance	Details
	<p>4. Establish a centralized site on the NIH Home Page for access to NIH materials in Spanish.</p>	<p>Corazon” was completed.  Target met. A centralized site was established and launched in October 1998.</p>	
<p><b>c) Increase awareness of NIH-sponsored research results among the general public.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Increase awareness about the importance of milk, sources of calcium, and ideas for incorporating calcium into the diet among young people and their parents.</li> <li>2. Increase awareness among the general public about the symptoms of stroke and the need to seek treatment rapidly.</li> <li>3. Use age-appropriate modules (Internet) to increase older adults awareness of health information and, based on NIA supported cognitive research findings, enhance the online learning experience for people of age 50 and over.</li> <li>4. Expand MEDLINEplus, NLM’s consumer health information service, to enhance services available to the general public – to include links to local, state, and inter-state health information; important health news items from the daily news media; and at least 15 percent of documents and links to consumer health information in languages other than English.</li> <li>5. Increase awareness of advances in diagnosis, treatment, and prevention of immune-mediated diseases (e.g., autoimmune diseases, asthma, allergic diseases, and graft rejection) among the general public, particularly youth.</li> <li>6. Increase awareness among the general public of new strategies to prevent and treat AIDS and its associated cancers and opportunistic infections.</li> <li>7. Increase awareness among the general public of research findings</li> </ol>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p>	<p>Page 169</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>about infectious pathogens and their vectors that predict and prevent conditions that lead to human diseases (e.g., antibiotic resistance, role of infectious pathogens in chronic disease, bioterrorism).</p> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Increase awareness among university presidents, program planners, and policy makers about college drinking and related problems.</li> <li>2. Increase awareness among the general public about the achievements of publicly-funded vision research.</li> <li>3. Increase awareness among young people of the importance of calcium in their diet.</li> <li>4. Increase the number of people who know the symptoms of stroke and rapidly seek treatment.</li> <li>5. Increase the public's understanding of cancer research, advances, and opportunities.</li> <li>6. Increase awareness among the general public that drug addiction is a brain disease.</li> <li>7. 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.</li> <li>8. 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.</li> </ol> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>1. Generate a minimum of 30 million</li> </ol>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target met. Mass media</p>	

Performance Goals	FY Targets	Actual Performance	Details
	<p>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.</p> <p>2. 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.</p> <p>3. Increase collaboration with professional associations of journalists, science writers, and health communicators to increase their coverage of NIH-funded research results.</p> <p>4. 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.</p> <p>5. Ensure that no less than 85 percent of respondents to a customer feedback instrument rate NLM services at least satisfactory.</p> <p>6. Increase the usage of NLM's existing catalog-based databases for books, serials, and audiovisuals by 15 percent.</p>	<p>activities to raise awareness generated more than 30 million media impressions.</p> <p>Target met. In FY 2000, new educational materials were developed, strategic alliances formed with professional organizations, and materials distributed to peer and opinion leaders.</p> <p>Target met. In FY 2000, NIH collaborated with these organizations to increase the likelihood that medical research findings will be reported in the media or through health communication programs.</p> <p>Target met. By September 2000, 78 organizations had joined the coalition.</p> <p>Target significantly exceeded. A survey showed that 98% of users rated NLM services as satisfactory or better.</p> <p>Target significantly exceeded. In FY 2000, the level of usage increased by 27% over the FY 1999 level.</p>	



Performance Goals	FY Targets	Actual Performance	Details
	<p>7. Increase the number of "health topics" in the Web-based MEDLINE plus to 300.</p> <p><b>FY 1999</b></p> <p>1. Develop and implement NIH information, education, and outreach programs on specific health issues: Low Vision.</p> <p>2. Increase the availability of consumer health information, publications, and reports under NIH's Centralized Consumer Health Information area by 20 percent.</p> <p>3. Complete the restructuring of NIMH's mental health education and information dissemination programs - -as recommended by reviewers and the National Advisory Mental Health Council.</p> <p>4. 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.</p> <p>5. Provide a single toll-free telephone number to reach NLM customer service staff.</p> <p>6. Implement a system to track customer service interactions, measure response times, and record customer feedback on NLM products and services.</p>	<p>Target significantly exceeded. MEDLINE plus contained 414 topics as of September 2000.</p> <p><b>FY 1999</b></p> <p>Target met. The Low Vision program was launched in October 1999.</p> <p>Target significantly exceeded. The number of on-line publications increased around 76% in 1999.</p> <p>Target met. A new Associate Director position was established and filled, along with a new mission statement for the Institute's communications programs.</p> <p>Target met. NIDDK established relationships with 375 public and private organizations to support the National Diabetes Education Program.</p> <p>Target met. The toll-free telephone line was established.</p> <p>Target met. NLM installed software and a program that tracks inquiries, measures response times, and records customer feedback on its services.</p>	
<p><b>d) Increase awareness of clinical research and support participation in clinical trials.</b></p>	<p><b>FY 2002</b></p> <p>Increase awareness of NIAMS-sponsored clinical research and generate interest in participating in clinical studies among minority populations.</p> <p><b>FY 2001</b></p> <p>1. Educate the public about the importance of NIMH-supported clinical research and interest individuals and their families in</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p>	<p>Page 178</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>participating in clinical studies.</p> <ol style="list-style-type: none"> <li>2. Increase the number of initial contacts about clinical trials with the Patient Recruitment and Public Liaison Office (PRPL).</li> <li>3. Improve NCI efforts to increase participation and retain minorities, under-served populations, and the elderly in clinical trials.</li> <li>4. Develop Web-based clinical trials tools that will improve the development, conduct, and ease of participation in NCI-sponsored clinical trials.</li> </ol> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>3. 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.</li> <li>4. Increase visitors to NCI's cancerTrials Web Site 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.</li> </ol>	<p><b>FY 2000</b></p> <p>Target substantially met. The Constituency Outreach and Education Program (COEP) was initiated in early 2000.</p> <p>Target substantially met. Focus groups were conducted with individuals from a variety of backgrounds, including representatives of racial and ethnic minority groups, to understand the motivations and barriers to participation in specific clinical trials.</p> <p>Target met. NCI developed a simplified and easy to understand informed consent form.</p> <p>Target significantly exceeded. The total number of users has expanded by 33% and the range of information available on the Web site has been considerably enlarged.</p>	

Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 1999</b> Initiate a broad-based communications and public outreach program to reach physicians, and eventually, community groups and the general public.</p>	<p><b>FY 1999</b> Target met. A broad-based communications and public outreach program was initiated in the 3rd quarter of FY 1999</p>	
<p><b>e) Establish a Clinical Trials Database, as required by the FDA Modernization Act.</b></p>	<p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Promote the database as a resource for patients, physicians, researchers, community health groups and others.</li> <li>2. Complete an implementation study to determine the optimal design and function of a toll-free telephone to facilitate access to information in the Clinical Trials Database.</li> <li>3. Expand the number of industry-sponsored clinical trials in the database by 250 and the number sponsored by other federal agencies by 100.</li> </ol> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>1. Expand the Clinical Trials Database to include trials from other federal agencies and the private sector.</li> <li>2. Develop options for implementation of toll-free telephone access to information in the Clinical Trials Database.</li> </ol> <p><b>FY 1999</b> Develop and implement the Clinical Trials Database.</p>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target met. 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.</p> <p>Target substantially met. An initial implementation report, including possible implementation strategies, was received from the contractor soon after the close of FY 2000. A final report is near completion.</p> <p><b>FY 1999</b> Target met. Data elements were developed for the database based on the legislative requirements and discussions with collaborating NIH Institutes and other groups.</p>	<p>Page 183</p>

**Performance Goal Details - Communication of Results**

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

**Performance Targets & Results****FY 2002**

1. Encourage the use of NINR-supported health care research findings in symptom management, health promotion, and disease prevention among health care practitioners.
2. Communicate the results of research and collaborative activities that will accelerate the development of vaccines for emerging diseases and the application of vaccine strategies in less traditional areas (e.g., chronic diseases, autoimmune diseases, bioterrorism).

*Performance to be reported in February 2003.*

**FY 2001**

1. 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.
2. 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.
3. Increase awareness of NIDA-sponsored clinical treatment among health care providers.
4. 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.
5. Complete the expansion of 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.

*Performance to be reported in February 2002.*

**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.

*Performance: Target met. Model case studies on 11 aspects of treatment for cardiovascular disease (CVD) in African-American patients have been developed and are now being converted into interactive Web-based continuing education programs for physicians and nurses that will offer continuing education credits. Physicians who treat African-American patients have reached more than 600,000 other health*

### Performance Targets & Results

*professionals, patients, and members of the public with guidelines-based messages about treating high blood pressure, high blood cholesterol, and other cardiovascular disease (CVD) risk factors.*

2. Fund a series of demonstration projects applying telemedicine and other technology to improve the speed of reaching heart attack victims with lifesaving treatment.

*Performance: Target met. Ten project awards were made, including traditional informatics projects and to explore the potential of high tech applications to expedite the recognition and treatment of heart attack patients.*

3. 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 Web site components that will allow users to interact on-line with live discussions, conferences, and other types of meetings.

*Performance: Target substantially met. Enhanced electronic outreach, on-line access to educational conferences, and a National Institute of Nursing Research listserv were all created.*

4. 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.

*Performance: Target not met. Planning and preparation for the mammography campaign to reach health professionals are still under way. The intended research and evaluation components are under way and will continue in FY 2001.*

5. Complete the evaluation of selected NIH outreach programs: a) 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, and b) the use of clinical practice guidelines on high blood pressure and obesity.

*Performance: Target met. a) The evaluation was completed as part of the activities described in FY 2000 target 1 above. b) Focus groups with physicians, patients, and allied health personnel to evaluate whether physicians are using the guidelines were completed in the Spring of 2000. An analysis of initial summary data was completed as well. Plans are to submit final report to a refereed journal of Spring 2001. The Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report has now been formatted into multiple products for primary care providers. As measured by hits on the NHLBI’s “Aim for a Healthy Weight” Web Site and requests for copies, these products are being widely used.*

#### FY 1999

1. Evaluate several selected NIH outreach programs: a) 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, and b) the use of clinical practice guidelines on high blood pressure and obesity.

*Performance. Target not met. The outreach effort is scheduled to run an additional year. Accordingly, the planned evaluation is still under way. Some preliminary data*

<b>Performance Targets &amp; Results</b>
<p><i>have been received. Once the outreach effort has been concluded (in FY 2000), the final evaluation will be finished.</i></p> <p><i>a) An evaluation of physician practices in hypertension treatment began in the summer of 1999 with a series of eight focus groups with physicians, patients, and allied health professionals. Because of weather and unanticipated travel problems physician recruitment proved more difficult than anticipated. It is now planned that the focus groups will be completed in spring 2000. b) The work on the Practical Guide to the Identification, Evaluation, and Treatment of Overweight and Obesity is nearing completion. The final document should be available early in 2000 and will be disseminated through the various associations working on the Guide as well as by the NHLBI. The full Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity: Evidence Report was also formatted as an electronic text book that will be made available through the NHLBI Website. A CME component may be added. The use by primary care physicians of the various formats of the obesity guidelines will be examined.</i></p>

Note: FY 2000 target #5 incorporated a revised plan for the corresponding FY 1999 target that was not completed in that year.

### ***Goal Background***

NIH's research mission -- to develop new knowledge that leads to better health -- is dependent upon the translation of research advances into improved patient care. This goal significantly contributes to that translation, since the first step in the "chain of events" in utilizing research results to improve patient care, begins with awareness and ensuring that health care providers learn about the latest research findings.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

The principal measures of achievement for each of these targets is implementing the project and tracking and measuring the effects of the outreach, education, and informational activities. Where relevant, the use and usefulness of communication materials, telemedicine, and Web technology will be assessed.

#### ***Validation and Verification:***

Project implementation and impact findings will be confirmed in written documentation.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results*****Target 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.**

Target met. In FY 2000, the Association of Black Cardiologists (ABC), with whom the NHLBI contracted in FY 1999, identified 11 key aspects of treatment for African-American patients with cardiovascular disease – for example, high blood pressure, heart attack warning signs -- and developed model case studies on each. These case studies are now being turned into Web-based interactive self-study programs that will offer CMEs. They are expected to be online by early April 2001.

Previously, the ABC had assumed responsibility for the National Physicians Network (NPN), a multidisciplinary group of physicians formed by the NHLBI in 1995 to carry out community-based heart health education for professionals, patients, and the public. Within the first 15 months of the project, NPN members had reached an estimated 595,000 health professionals and members of the public with messages about appropriate treatment for cardiovascular disease: 420,000 through traditional speaking events at which slides from an online ABC Speakers' Kit were frequently used, and 175,000 through a New Orleans PBS TV medical talk show targeting blacks that aired repeatedly over several weeks.

Assessment Data: NPN members submit a reporting form for each presentation, which includes information on the number and type of audience attending. The ABC's Webmaster tracks the number of downloads of the slides in the Speakers' Kit from the Website, <http://www.abcardio.org/>.

**Target 2: 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. Five awards were made for traditional informatics projects. An additional five awards were made for projects to explore high technology applications related to expediting the recognition and treatment of patients with a heart attack.

The National Library of Medicine issued an RFP in May 1998 for project plans for "Informatics for the National Heart Attack Alert Program (NHAAP)." This was done with the support of NHLBI, which coordinates the NHAAP. In FY 2000, five groups were awarded contracts that address "mainline" informatics projects. An additional five awards were made for high technology applications related to improving the speed of reaching heart attack victims with lifesaving treatment.

Assessment Data: Individual projects evaluate and report progress in meeting their goals on a quarterly basis to NLM. The projects are summarized on the NLM Website at <http://www.nlm.nih.gov/ep/nhaap.html>.

**Target 3: Use telehealth technology and TV cable networks to mount education projects with nursing organizations and academic institutions -- broadcast select conferences and workshops to nursing organizations and academic institutions, add components to the National Institute of Nursing Research Web site that will allow users to interact on-line through participation in on-line live discussions, conferences, and other types of meetings.**

Target substantially met. Enhanced electronic outreach, on-line access to educational conferences, and a National Institute of Nursing Research NINR listserv were created.

The NINR made use of Internet capabilities to strengthen communication with nursing organizations and academic institutions.

An e-mail listserv – “News from NINR,” established in FY 1999 -- became fully operational in FY 2000. This listserv provides an electronically accessible way to report on NINR activities, including conferences, program announcements and appointments. There are presently more than 2,000 addresses -- over 1,400 schools of nursing across the nation and numerous clinical sites that can potentially benefit from the listserv. In FY 2000, the public affairs addresses were expanded from 5 to 72.

NINR held a workshop (cosponsored by two other nursing organizations) in September 2000, called “Making Today’s Research Tomorrow’s Headlines and Success Stories from the Field.” The workshop’s 150 attendees heard from media experts and media-experienced nursing researchers. The workshop was filmed, and NINR has used the listserv and e-mail addresses of public affairs officers at schools of nursing to disseminate the Internet address (URL) where the video of the event can be accessed.

Also, an education seminar entitled “Research Training: Developing Nurse Scientists,” held at NIH in July 2000 and attended by 40 students, will soon be available on-line for continuing education credits. A contractor is readying the filmed program for Web access, and the nursing community will be alerted to its availability through the listserv. NINR had hoped the program would be completed by the end of FY 2000, but anticipates that the seminar will be available on-line by Spring of 2001. At that time, it is envisioned that a once-a-month chat room will be established where program directors will be available to answer questions from nursing students and nurse researchers, which was a goal for 2000.

Assessment Data: Internal data available to NINR provides figures on the number of Website hits, the number of attendees of events, and the number of addresses in the listserv.

**Target 4: Expand the “Not Just Once, But for A Lifetime” mammography campaign to reach health professionals 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.**

Target not met. Planning and preparation for the mammography campaign to reach health professionals is still under way. The intended research and evaluation components are under way and will continue in FY 2001.

Preliminary review of the literature on how to reach health professionals has been completed and plans are underway to conduct focus groups/interviews with health professionals to assess their information needs and interests.

A mammography tear-off pad is being revised to include information about Medicare coverage of mammograms, and will be printed and distributed to providers, and promoted to health professional organizations, the Health Care Financing Administration networks, and others.

Literature reviews have been conducted to assess awareness and determine appropriate communication strategies; omnibus surveys and focus groups have been used to establish baseline awareness and attitudinal data. Omnibus surveys and focus groups will be used again in the future to measure outreach efforts and to assess changes in awareness among target audiences. While over 75% of the women surveyed in 1999 were aware that Medicare will cover the cost of mammograms, minority women are nearly twice as likely to be unaware of this benefit.

Assessment Data: The data reported above come from “Knowledge, Attitudes, and Behavior of Women Ages 65 and Older on Mammography Screening and Medicare: Results of an Omnibus Survey,” National Cancer Institute, July 1999.

**Target 5: Complete the evaluation of selected NIH outreach programs: a) 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, and b) the use of clinical practice guidelines on high blood pressure and obesity.**

Target met.

a) This evaluation envisioned by this target has already been discussed above in the FY 2000 assessment for Target 1.

b) Focus group research with physicians, patients, and allied health personnel to evaluate whether physicians are incorporating the information from the NHLBI’s *Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI)* into their practices was completed in the Spring of 2000. A working group comprised of clinicians, survey research, and public health experts reviewed an analysis of the initial summary data results the following Fall. A full, final report is now being prepared and is expected to be ready for submission to a refereed journal by Spring 2001.

The *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report* has now been formatted into multiple products that make the information in the guidelines simple and practical for primary care providers. These products are being disseminated or will shortly be disseminated to physicians by their professional organizations. They also are now available or about to be available through the NHLBI's new "Aim for a Healthy Weight" Web site, [http://www.nhlbi.nih.gov/health/public/heart/obesity/lose\\_wt/index.htm](http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm).

The products include the *Practical Guide to the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*, done in collaboration with the North American Association for the Study of Obesity (NAASO), as well as a slide show, an electronic textbook, and a hand-held Palm pilot application.

The professional organizations that have agreed to promote the Guidelines to their members include the American Medical Association (AMA), the American Diabetes Association (ADA), the American Academy of Family Physicians (AAFP), and NAASO. The AMA has written about the Guidelines in its publication, *American Family Physician*; the AAFP has information from the Guidelines on their Web Site; and the ADA has not only printed numerous articles on the Guidelines in their various publications but also is using them in their Weight Certification Program. The Guidelines also are being utilized in obesity training programs for physicians, nurses, and dietitians that are being conducted by the 7 Centers for Obesity Research and Education (CORE), which also are conducting evaluations of the impact of the training sessions on health providers' practice behaviors and attitudes.

The online professional education products, along with consumer-oriented obesity education products, have been quite sought after as measured by hits on the NHLBI site and requests for the original Guidelines Evidence Report and its Executive Summary, released in 1997; in the past year 900 requests for the guidelines and 160 for the executive summary were received. The CORE directors are also collecting data on changes in physician practices in treating overweight and obese patients.

Assessment data: Working Group Report on Critical Factors in Hypertension Control: Assessment of Knowledge, Attitudes and Practices, September 26, 2000, Bethesda, MD. American Medical Association, American Diabetes Association, American Academy of Family Physicians, North American Association for the Study of Obesity, Centers for Obesity Research and Education; and NHLBI "Aim for a Healthy Weight" Web Site, [http://www.nhlbi.nih.gov/health/public/heart/obesity/lose\\_wt/index.htm](http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm).

### ***Progress Toward Goal Achievement***

Substantial progress has been made toward the goal of increasing awareness of selected NIH-sponsored research among health professionals. NIH has established relationships with provider organizations; identified most effective ways to communicate to health professionals; funded

new demonstration projects to improve access to NIH medical treatment information; and developed information products for health professionals.

***Next Steps***

Planned expansion of outreach to health professionals to raise awareness about mammography among women 65 and over, as well as using technology to reach nursing researchers, practitioners, and students, though not completed at this time, are well under way and are expected to be completed in the near future. In future years efforts will be expanded to include more topics of NIH-sponsored research as well as additional strategies to reach health professionals.

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

**Performance Targets & Results**

**FY 2002**

1. Use NHLBI Enhanced Dissemination and Utilization Centers for asthma and cardiovascular disease to help decrease the excess mortality from these conditions in high risk communities.
2. Increase awareness of the health implications of obesity to high risk, affected publics, such as African American women, and increase understanding about the health risks of overweight.
3. Increase awareness of osteoporosis and related bone diseases in Hispanic and Asian individuals.
4. Encourage prevention and management of chronic illnesses, e.g., diabetes and arthritis, among the nation's Hispanic populations.
5. Develop and implement eye health awareness campaigns that target minority and underserved populations.
6. Raise awareness of the benefits of vision rehabilitation among people over 65 and minority and underserved populations.

*Performance to be reported in February 2003.*

**FY 2001**

1. Develop and implement an AIDS vaccine communication campaign to increase awareness of AIDS vaccines before the initiation of a large efficacy trial.
2. Increase understanding about the seriousness of diabetes and the importance of blood glucose control among African Americans, Asian/Pacific Islanders, and American Indians.
3. Increase awareness of autoimmune diseases (such as rheumatoid arthritis, lupus, and scleroderma) among minority populations who are disproportionately affected.
4. Increase awareness of sports injury prevention among parents.
5. 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.
6. Increase knowledge among Hispanic parents of the effects of drugs on the brain and encourage them to talk with their children about drug abuse.
7. Increase awareness of the effects of drug abuse among Native American Indians.

*Performance to be reported in February 2002.*

## Performance Targets & Results

### FY 2000

1. Increase the available information on the benefits of exercise to older people.  
*Performance: Target met. Information about the benefit of exercise was made available through the news media, health fairs, and professional meetings.*
2. Develop and disseminate motivational messages related to breast and cervical screening to African American, Hispanic, and Asian communities.  
*Performance: Target met. Motivational messages on breast and cervical cancer screening are being disseminated to African American, Hispanic, and Asian communities.*
3. Expand programs on anxiety disorders and depression to audiences for whom language or literacy are challenges.  
*Performance: Target met. NIMH has developed a series of five easy-to-understand booklets on anxiety disorder. Similar materials for depression and bipolar disorder are under development.*
4. Develop and disseminate easy-to-read and Spanish language health education materials on health issues to targeted special populations.  
*Performance: Target met. Several NIH Institutes developed and disseminated easy-to-read and Spanish language materials on various diseases and other health topics.*
5. Develop and implement diabetes awareness campaigns that target minority populations and their health care providers.  
*Performance: Target met. Seven diabetes awareness campaigns targeting minority populations and seniors were developed and implemented.*
6. 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.  
*Performance: Target not met. The media summit was held, but not until December 1, 2000. The planning for this meeting was completed in FY 2000.*
7. Pursue new outreach and collaboration initiatives to disseminate information and resources on rheumatic diseases in minority populations.  
*Performance: Target met. An African American Community Partnership has been launched.*

### FY 1999

1. Develop and implement NIH information, education, and outreach programs on specific health issues: Breast Cancer and Mammography Education Program.  
*Performance: Target met. The National Cancer Institute (NCI) continued to implement the Breast Cancer and Mammography Education program, increasing outreach to include Cancer Information Service offices and HCFA partners.*

### Performance Targets & Results

2. Develop and implement NIH information, education, and outreach programs on specific health issues: extend the “Back to Sleep Campaign” to minority populations.

*Performance: Target met. Major FY 1999 accomplishments in the “Back to Sleep Campaign” were:*

- Completed a video featuring a series of vignettes of minority families overcoming some of the barriers to placing an infant on their back to sleep.*
- Implemented outreach to day care facilities.*
- Created coalition of African American organizations who made a commitment to devote the resources of their organizations to promoting back sleeping in African American communities.*

3. Evaluate several selected NIH outreach programs: cardiovascular health outreach activities for Latinos.

*Performance: Target met.\* However, an evaluation of the community-based outreach initiative “Salud para Su Corazon” (Health for your heart) was completed.*

4. Establish a centralized site on the NIH home page for Access to NIH materials in Spanish.

*Performance: Target met. A centralized site was established and launched in October 1998.*

Notes: \*NIH’s Assessment Report for FY 1999 erroneously listed FY 1999 target #3 as “not met.” *Salud para Su Corazon* is presently NIH’s only cardiovascular health outreach program for Latinos. Completing the evaluation of this program in FY 1999 represented full achievement of the intended target in that FY.

### **Goal Background**

Many 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 be regularly encountering a health care provider. Furthermore, often broadly applicable research results are less likely to reach and benefit certain underserved (often high risk) publics. Accordingly, directly addressing “health disparities” – whether the differential incidence or risk of disease among population segments or the access to health care – is an identified priority of NIH.

This goal contributes to this purpose by ensuring that the individuals who are most likely to benefit—and those least likely to readily become aware-- are specifically targeted with information resulting from pertinent research results.

### **Performance Assessment Approach**

#### *Basis and Data:*

The principal measures of achievement for each of these targets is implementing the project and tracking and measuring the effects of the outreach, education, and informational activities.

Where relevant, the use and usefulness of communication materials, telemedicine, and Web technology will be assessed.

*Validation and Verification:*

Project implementation and impact findings will be confirmed in written documentation.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

#### **Target 1: Increase the available information on the benefits of exercise to older people.**

Target met. Information about the benefit of exercise was made available in the news media, at health fairs, and at professional meetings.

NIA convened a panel of experts to decide upon an appropriate research-based prescription for exercise for people over 50. The program, based entirely on research funded by NIA and other NIH Institutes, includes endurance, strength, balance, and flexibility programs, as well as motivational material and nutrition information.

NIA has published a 100 page primer, *Exercise: A Guide from the National Institute on Aging*, to publicize these findings. 350,000 copies of this book have been produced and distributed. In addition, NIA and NASA produced a special edition with John Glenn on the cover – distributed at the time of Glenn's recent space shuttle flight.

NIA's book has been widely promoted in the press and reviews have been excellent. Single copies are available free of charge by calling NIA's toll-free line. A video companion to the guide has been prepared and is also now available. NIA is selling the companion video for a small fee in order to recover costs sufficient to keep it in circulation. NIA is also investigating commercial avenues that would enable wider distribution.

This publication is the most frequently visited document on NIA's Web site. Also, the television public service announcement NIA produced to promote the book received the equivalent of several million dollars in free air time and an Emmy nomination.

Assessment Data: The book can be ordered from NIA by phone at 1-800-222-2225 or viewed on the Internet at [www.nih.gov/nia/healthpubs/nasa-exercise/](http://www.nih.gov/nia/healthpubs/nasa-exercise/).

#### **Target 2: Develop and disseminate motivational messages related to breast and cervical screening to African American, Hispanic, and Asian communities.**

Target met. Motivational messages on breast and cervical screening are being disseminated to African American, Hispanic, and Asian communities.

*Breast Cancer.* Focus groups were conducted with older women, including African Americans, Hispanics, and Asian women, to test motivational messages on breast cancer and mammography screening. Based on this information, plans are underway to develop additional resources to motivate minorities, high risk, underserved, and older women to get screened for breast cancer. Additionally, brochures and posters targeting Asian women developed by a Health Care Financing Administration grantee are being pretested nationally and will be produced for national distribution. The program continues to promote breast cancer and mammography materials to these audiences through the NCI's Cancer Information Service outreach partners, and special promotions through the media, particularly minority media.

*Cervical Cancer.* Focus groups were conducted with older women to test motivational messages on cervical cancer and the Pap test. Based on this information, a new brochure was developed for older women. Additionally, a new graphic design, which was tested in mall-intercept interviews with women, was developed and adapted to all NCI cervical cancer materials, including African American and Hispanic materials.

A new NCI Vietnamese Pap screening brochure was adapted from a brochure created by the Vietnamese Health Promotion Project, an NCI grant recipient. NCI worked closely with their staff to design and update the brochure for national distribution.

Additionally, a health professional pad with tear sheets was developed. The tear sheets, which are designed for health professionals to give women patients include information on the importance of Pap screening as well as a Pap test appointment reminder. The pad, which was pretested with health professionals and women, is also being translated into Spanish.

Assessment Data: NCI internal data, including Cancer Information Service database. Hard copies of the research reports are available through NCI's Office of Communications.

**Target 3: Expand programs on anxiety disorders and depression to audiences for whom language or literacy are challenges.**

Target met. NIMH has developed a series of easy-to-understand booklets on mental disorders. The first five booklets in the series (printed in October 2000) are on Anxiety Disorders – “The Anxiety Disorders: Real Illnesses” series includes: *Generalized Anxiety Disorder, Panic Disorder, Obsessive-Compulsive Disorder, Post-traumatic Stress Disorder, and Social Phobia.*

Developed with guidance from a nationally recognized health literacy expert, these materials were pre-tested with anxiety disorder patients at an outpatient clinic and with GED students in an adult basic education class.

Distribution for these booklets has been expanded to include NIMH's Constituency Outreach and Education Program Partner's state and community organizations, as well as meetings, conferences, workshops, and the NIMH Web site and fax back system.



The next step is the development of two easy-to-understand booklets on depression and bipolar disorder. These are expected to be ready for distribution by summer 2001.

Assessment Data: Distribution data for these publications are maintained by the Information Resources and Inquiries Branch, NIMH. The publications can be found on the NIMH Web site at <http://www.nimh.nih.gov/anxiety/realillness>.

**Target 4: Develop and disseminate easy-to-read and Spanish language health education materials on health issues to targeted special populations.**

Target met. Several NIH Institutes developed and disseminated easy-to-read and Spanish language health education materials. NIMH produced a series of health education materials in easy-to read Spanish, which are in distribution to targeted special populations. NIDDK developed and disseminated easy-to-read and Spanish language materials on diabetes, hepatitis, and urologic and kidney diseases. NIAMS developed and widely disseminated Spanish language informational materials on arthritis, lupus, and osteoporosis.

NIMH's "The Anxiety Disorders: Real Illnesses" series has been translated into Spanish language. NIMH utilized the professional services of an expert translation service, and followed up with reviews (pre-tests) by several Spanish language professionals and laypersons to ensure that the tone, meaning, and understandability of the booklets were not lost with translation.

These materials are currently being distributed through several mechanisms: 1) the NIMH Constituency Outreach and Education Program (COEP), where Outreach Partners are initiating outreach programs to special populations identified in their communities (i.e., literacy challenged and Spanish-speaking populations; 2) the Consumer Information Center's (CIC) annual distribution program that targets over 30,000 Spanish consumer and membership organizations -- which include health and mental health clinics, Hispanic advocacy groups, private practice physicians, professional and women's organizations, etc.; 3) CIC's "Revisita Catalog," a listing of Spanish language materials available throughout the federal government, and 4) the NIMH home page which makes these materials available through a centralized site and its fax back system.

Assessment Data: The publications can be found on the NIMH Web site at <http://www.nimh.nih.gov/anxiety/realillness.cfm> or through its fax back system "Mental Health FAX4U" at 301-443-5148. Information on distribution is collected and maintained by the NIMH Information Resources and Inquiries Branch.

NIDDK has developed and distributed easy-to-read and Spanish language health education materials in the areas of diabetes, hepatitis, and urologic and kidney diseases. In FY 2000, for example, NIDDK produced an easy-to-read diabetes complications booklet series that was distributed through the NIDDK clearinghouse in response to inquiries from the public and through conferences. NIDDK disseminated approximately 143,770 easy-to read English and

41,5000 Spanish publications on diabetes. In the area of hepatitis, over 105,000 English and 26,000 Spanish publications were disseminated, and in urologic and kidney diseases, 3,968 English publications were distributed.

Assessment Data: The materials are available through NIDDK's three clearinghouses, as well as on the NIDDK Website at [www.niddk.nih.gov](http://www.niddk.nih.gov). The information on dissemination was gathered through inventory tracking mechanisms at the three NIDDK clearinghouses.

NIAMS has developed a bilingual (Spanish/English), easy-to-read booklet on arthritis. Also, Spanish language handouts on lupus and osteoporosis were refined. 92,000 copies of these booklets were distributed in 200 U.S. markets in FY 2000. A Hispanic/Latino Health Educator was hired in September 2000 to further develop materials and work with community and national organizations, to improve dissemination and development of more effective ways to reach and inform this population. A toll-free number for the NIAMS clearinghouse, with a Spanish language option, was added to improve access to NIAMS materials.

Assessment Data: Data on requests for these publications are maintained by NIAMS clearinghouses and also (for the arthritis booklet) the Federal Consumer Information Center. The URL of the arthritis booklet is <http://www.nih.gov/niams/healthinfo/tengo.htm>, and the URL of the osteoporosis fact sheet is <http://www.osteoporosis.org/a139sp.html>. The toll free number is given at <http://www.nih.gov/niams/healthinfo/info.htm>.

**Target 5: Develop and implement diabetes awareness campaigns that target minority populations and their health care providers.**

Target met. Seven diabetes awareness campaigns targeting minority populations and seniors were developed and implemented.

Seven diabetes awareness campaigns were either launched or revised for the following target audiences: African Americans, American Indians, Asian Americans, Hispanic/Latinos (in both English and Spanish), and older Americans. The campaigns and materials have reached the intended target audiences.

The TV public service announcements (PSAs) have generated close to \$5 million in free air time the past year. (This is the equivalent value of the advertisements if the air time had been purchased.) The print PSAs reached a circulation of over 5 million people. The radio PSAs have generated over \$1 million of free air time. Furthermore, approximately 200,000 pieces of campaign materials have been mailed in the past year.

Assessment Data: The following companies collected data on when and where the public service announcements were played and how many people were reached. Goodwill Communications, West Glen Communications, Bienestar LCG Communications, and PCS/JWJ Television tracked the TV PSAs. West Glen Communications, Bienestar LCG Communications and News

Generation Inc. tracked the radio PSAs, and Bienestar LCG Communications, Bacon's and Burrelle's media services tracked the print placements.

**Target 6: 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.**

Target not met. Plans for conducting the NIH Spanish-Language Media Roundtable were finalized in FY 2000. However, the event was not held until December 1, 2000.

In FY 2000, the HCI convened an ad hoc planning group, comprised by NIH Information Officers and key Hispanic community representatives. In addition, a "mini-assessment" was implemented to query potential participants regarding their experiences and knowledge of Hispanic media and NIH Information Offices. Meeting plans, materials, and logistics were finalized with the input of the planning group and other NIH staff.

Assessment Data: Documentation for the Roundtable (agenda, participant list, and draft proceedings) is available from NIH's Office of Communications and Public Liaison.

**Target 7: Pursue new outreach and collaboration initiatives to disseminate information and resources on rheumatic diseases in minority populations.**

Target met. An African American Community Partnership has been launched.

The Local Health Partnership Program (HPP), A NIAMS Diversity Outreach Initiative, began in February 2000. The purpose of the program is to work together with community leaders and organizations that represent both the African American and Hispanic/Latino communities in a metropolitan area, to develop a model community-based program that will begin to address the disparities in rheumatic diseases that exist in these populations.

In FY 2000, 25 individuals representing 22 local community organizations met from the African American community to help co-author the HPP Plan. In addition, another group composed of 15 present and former NIH Clinical Center patients from the community provided their perspectives on NIAMS programs and services. A Community Forum on the model community-based program was held to gather additional community input. Community presentations have begun and additional talks have been scheduled.

A Program Coordinator and a Hispanic/Latino Health Educator have been hired to manage and evaluate the initiative. Plans are being developed for a Hispanic/Latino community partnership.

Assessment Data: Detailed updates and reports are distributed via e-mail to HPP Partners and NIAMS staff to document progress and help facilitate evaluation. Articles on progress also appear periodically on the NIAMS and NIH Web sites. For examples, see the NIAMS intramural research

newsletter at [http://www.nih.gov/niams/news/sum2000/summer\\_2000.htm](http://www.nih.gov/niams/news/sum2000/summer_2000.htm) and the NIH Record story at [http://www.nih.gov/news/NIH-Record/07\\_11\\_2000/story04.htm](http://www.nih.gov/news/NIH-Record/07_11_2000/story04.htm)

### ***Progress Toward Goal Achievement***

Many of NIH's Institutes are accelerating their efforts to reach out to high risk, underserved, and other affected populations with intensified health education programs. These populations include older Americans, persons with low literacy skills, and minority populations. Demonstrated success in meeting targets such as these can be expected to contribute to improved health status in these important populations in the future.

### ***Next Steps***

Reaching minority and underserved populations is a high priority for all of NIH's Institutes and Centers, as reflected in their strategic plans to reduce or eliminate health disparities and in their communication activities. Even where targets have been met, the Institutes/Centers plan to continue their efforts to reach these populations. The Institutes will also include additional health topics, additional partnerships, and additional affected audiences as these efforts expand in coming years.

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

**Performance Targets & Results**

**FY 2002**

1. Increase awareness about the importance of milk, sources of calcium, and ideas for incorporating calcium into the diet among young people and their parents.
2. Increase awareness among the general public about the symptoms of stroke and the need to seek treatment rapidly.
3. Use age-appropriate modules (Internet) to increase older adults awareness of health information and, based on NIA supported cognitive research findings, enhance the online learning experience of people of age 50 and over.
4. Expand MEDLINEplus, NLM's consumer health information service, to enhance services available to the general public – to include links to local, state, and inter-state health information; important health news items from the daily news media; and at least 15 percent of documents and links to consumer health information in languages other than English.
5. Increase awareness of advances in diagnosis, treatment, and prevention of immune-mediated diseases (e.g., autoimmune diseases, asthma, allergic diseases, and graft rejection) among the general public, particularly youth.
6. Increase awareness among the general public of new strategies to prevent and treat AIDS and its associated cancers and opportunistic infections.
7. Increase awareness among the general public of research findings about infectious pathogens and their vectors that predict and prevent conditions that lead to human diseases (e.g., antibiotic resistance, role of infectious pathogens in chronic disease, bioterrorism).

*Performance to be reported in February 2003.*

**FY 2001**

1. Increase awareness among university presidents, program planners, and policy makers about college drinking and related problems.
2. Increase awareness among the general public about the achievements of publicly-funded vision research.
3. Increase awareness among young people of the importance of calcium in their diet.
4. Increase the number of people who know the symptoms of stroke and rapidly seek treatment.
5. Increase the public's understanding of cancer research, advances, and opportunities.
6. Increase awareness among the general public that drug addiction is a brain disease.

### Performance Targets & Results

7. **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.**
8. **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.**

*Performance to be reported in February 2002.*

#### FY 2000

1. 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.

*Performance: Target met. Mass media activities to raise awareness of the importance of eating at least 5 servings of fruits and vegetables a day generated more than 30 million media impressions.*

2. 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.

*Performance: Target met. In FY 2000, new educational materials development, strategic alliances with professional organizations that interact with parents and children, and target distribution of materials to peer leaders and opinion leaders were implemented.*

3. Increase collaboration with professional associations of journalists, science writers, and health communicators to increase their coverage of NIH-funded research results.

*Performance: Target met. In FY 2000, NIH succeeded in collaborating with professional organizations of journalists, science writers, and health communicators to increase the likelihood that medical research findings will be reported in the media or through health communication programs.*

4. 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.

*Performance: Target met. The WISE EARS! campaign was launched in July 1999. Seventy eight organizations had joined the coalition by September 2000. Members included voluntary groups; state and local government agencies; national, regional, and local organizations; unions and industry groups; and organizations that advocate for children and older Americans.*

5. Ensure that no less than 85 percent of respondents to a customer feedback instrument rate NLM services at least satisfactory.

*Performance: Target significantly exceeded. A survey showed that 98% of users questioned rated NLM services as satisfactory or better, and 92% rated the services*

**Performance Targets & Results**

*as good or excellent.*

6. Increase the usage of NLM's existing catalog-based databases for books, serials, and audiovisuals by 15 percent.

*Performance: Target significantly exceeded. FY 2000 usage of NLM's catalog-based databases increased by 27% over the FY 1999 level.*

7. Increase the number of "health topics" in the Web-based MEDLINE *plus* to 300.

*Performance: Target significantly exceeded. MEDLINE plus contained 414 health topics as of September 2000.*

**FY 1999**

1. Develop and implement NIH information, education, and outreach programs on specific health issues: Low Vision.

*Performance: Target met. Development of the Low Vision Education Program was completed; implementation began with a program launch on October 15, 1999. Mass media materials were produced and distributed to the print media and by satellite to television and radio stations in all 50 states. A special emphasis was placed on the top 25 markets, plus markets with a large population of people aged 65 and older who are more likely to experience vision loss.*

2. Increase the availability of consumer health information, publications, and reports under NIH's Centralized Consumer Health Information area by 20 percent.

*Performance: Target significantly exceeded. The number of on-line publications increased from 144 in 1998 to 253 in 1999. This represents an increase of approximately 76%.*

3. Complete the restructuring of NIMH's mental health education and information dissemination programs.

*Performance: Target met. A new position with new responsibilities was created at the Associate Director level, with a joint appointment as Office Director. This position was filled in June 1998. A new mission statement for the Office was developed, and the new Associate Director made a presentation to the National Advisory Mental Health Council on her vision and goals for the Institute's communications program.*

4. 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.

*Performance: Target met. As one example, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has established relationships with 375 public and private organizations to support the National Diabetes Education Program. For NIDDK, organizations working with the Institute are regularly kept up-to-date about information and education activities. Materials are prepared to help interested organizations "get the message out" to their constituents and the general public. One measure of the intentions of these organizations to promote NIDDK messages is whether they order campaign kits. In 1999, partner organizations ordered 1,594 copies of the Campaign Guide for Partners. Other specialty campaign kits (the Medicare Benefits Campaign Kit, General Audience Campaign Kit, African American Media Kit, Asian*

### Performance Targets & Results

*American/Pacific Islander Media Kit, Hispanic/Latino Media Kit, American Indian Media Kit) became available in August 1999. By October 1999, nearly 2,500 of these specialty kits already had been requested from partner organizations.*

5. Provide a single toll-free telephone number to reach NLM customer service staff.

*Performance: Target met. A toll free number was established. Currently, the rate of callers on the toll-free number is more than 30,000 per year.*

6. Implement a system to track customer service interactions, measure response times, and record customer feedback on NLM products and services.

*Performance: Target met. NLM installed software (CustomerQ by Quintus Inc.) and has successfully implemented a program that tracks inquiries, measures response times, and records customer feedback on NLM services.*

Note: The FY 1999, 2000, and 2001 targets pertaining to the National Library of Medicine (NLM) were part of a separate NLM goal in the FY 2001 and earlier Annual Plans.

### Goal Background and Significance

This goal contributes to ensuring that new knowledge resulting from research is broadly disseminated to reach as many individuals who can benefit as possible. Often, the general 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.

### Performance Assessment Approach

#### *Basis and Data:*

NIH will track, document, and measure the effects of outreach, education, and information activities. The use and usefulness of communication materials will be evaluated. Participation in and the usefulness of telemedicine and Web technology will be examined.

#### *Validation and Verification:*

Project implementation and impact findings will be confirmed in written documentation.

### FY 2000 Performance Assessment

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#### *Discussion of FY 2000 Results*

**Target 1: Generate a minimum of 30 million media impressions through placements in newspaper 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 fruits and vegetables a day.**

Target met. Several different media activities were conducted throughout the past year. In just one campaign during a National “5 A Day Week” almost 30 million media impressions were generated.

Other activities include the development and distribution of a seasonal print media package and the Graham Kerr TV and radio segments, which were pretested with consumers and news directors. The 90-second TV segments are being played on 32 stations nationwide at least once a week. Two different radio flights were developed: a spring/summer and fall/winter, each with 39 segments. Each flight was distributed to approximately 1,500 stations and the spots are regularly playing on at least 100 stations, as well as several syndicated shows nationwide.

Awareness of the “5 A Day” message among the general public has risen from 8% in 1991 to 20% in 1999.

Assessment Data: The 30 million media impressions figure reported above is based on data from Burrelles Clipping Service. Knowledge and awareness data were obtained from the NCI document, “5 A Day for Better Health” program evaluation report, December 2000.

**Target 2: Expand the outreach of the Milk Matters campaign beyond parents and health professionals to focus directly on activities that help children and teens recognize the benefit of calcium in building strong bones.**

Target met. A series of new educational materials for children was developed (*Buddy Brush*, *Bone Up on Bone Loss*, and *Get Up and Grow*, all described below) were developed and distributed. These educational materials were developed for and with groups such as the American Academy of Orthopaedic Surgeons that interact with parents and children. The materials were distributed to peer leaders, opinion leaders, youth organizations, and interested young people.

A series of new calcium education products for children and their parents were developed in collaboration with strategic partners. Since calcium is important to healthy teeth, NICHD teamed with NIDCR to develop a coloring book for children. The coloring book, distributed through dentists offices, involves young children in learning why calcium helps build strong bones and teeth.

NICHD also formed an alliance with the American Academy of Orthopaedic Surgeon to develop a tear-pad of sheets called *Bone Up on Bone Loss*. The tear-pad was developed so that physicians and office staff could give a copy of the fact sheet to parents and that parents, in turn, could discuss calcium needs and sources with their children.

Another series of educational materials entitled *Get Up and Grow* were developed in collaboration with the education arms of the dairy industry. *Get Up and Grow* educational

materials, developed for parents and distributed through pediatricians and other health professionals, provide parents with ideas for increasing a child's calcium consumption. The materials feature a growth chart with the character Mario (from the Super Mario video game) drinking milk to develop strong bones.

By developing products with strategic allies, the Milk Matters campaign has been able to reach parents and children by distributing the new materials to the members of the organizations.

The Milk Matters campaign collected qualitative data from attendees at three professional conferences and quantitative data from customer satisfaction cards included in all Milk Matters material sent out from the NICHD clearinghouse. The qualitative data showed that users found the material useful and a useful educational tool for health professionals and parents. The quantitative data from the customer satisfaction cards revealed that the overwhelming number of respondents used the materials for in-school education programs and activities or for public education activities involving parents and children. Moreover, the data collected by the NICHD clearinghouse shows that, on average, 25,000 copies of the children's coloring booklet *Buddy Brush* were requested each month and 29,500 copies of Milk Matters for Your Child's Health were requested monthly. This pattern of usage provides evidence that health professionals, patients, and children used the educational materials in the way they were intended.

Assessment Data: Information about this campaign is available on <http://www.nichd.nih.gov/milk/milkqa.htm> The data reported above were collected from customer satisfaction "bounce-back" cards and NICHD Clearinghouse records.

**Target 3: Increase collaboration with professional associations of journalists, science writers, and health communicators to increase their coverage of NIH-funded research results.**

Target met. NIH succeeded in collaborating with professional organizations of journalists, science writers, and health communicators. These collaborations enhanced the positive relationship between the media and NIH and increased the likelihood that these reporters and writers accurately cover NIH-funded research.

In November 1999, several NIH information offices exhibited at the American Public Health Association's (APHA) annual meeting (with more than 7,000 in attendance), to reach health communicators and public health professionals with information about NIH communications and education programs.

In February 2000, NIH-- in collaboration with the National Association of Science Writers (NASW) -- hosted a day of workshops about the science being conducted at NIH. More than 160 reporters participated in the event.

In the spring of 2000, NIH collaborated with the University of Maryland's Knight Center for Specialized Journalism Fellowship Program to bring science reporters and scientists together. Seven NIH Institutes (NCI, NIDDK, NIAMS, NHGRI, NINDS, NIAAA, NICHD) hosted a

Knight Fellow for three weeks to learn more about NIH and its research (NCI hosted two fellows). The Fellows were reporters from national and regional media outlets, such as the Associated Press, Reuters, the St. Louis Post-Dispatch, the Dallas Morning News, and the Chicago Sun Times. NIDCR co-hosted a Knight Fellow with NIAMS. As a result, the July 2000 issue of *Orthopedics Today* featured a special report on "Engineering the Future of Orthopedics: The NIH and the Emerging Field of Tissue Engineering." The report contained several lengthy, excellent articles on NIH tissue engineering research.

Feedback from reporters who attended the NIH workshops and who participated in the Knight Fellowship program indicated an increased understanding and appreciation of NIH and its research. Newspaper article clippings and personal interactions with reporters following their participation in these collaborative activities indicated a greater understanding of NIH and how it works. Their experience also gave them new ideas for stories about NIH-funded research.

Assessment Data: APHA Conference Program includes information about NIH exhibitors and presenters. The NIH/NASW workshop materials (agenda, participant list, hand-outs) are available from NIH's Office of Communications and Public Liaison. The Knight Center produced an internal fellowship evaluation report.

**Target 4: Implement WISE EARS! communication 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.**

Target met. The WISE EARS! campaign was launched in July 1999. By September 2000, 78 organizations had joined the coalition. Members include voluntary groups; state and local government agencies; national, regional, and local organizations; unions and industry groups; and organizations that advocate for children and older Americans.

Mass media materials were developed and distributed to national and local print media and radio and television stations, including 1,064 newspaper articles that appeared in 32 states and potentially reaching a readership of 92.6 million people.

Resources provided to coalition members include the following: Web pages with information specifically oriented to parents, kids and teachers, and the public; use of the WISE EARS! logo, and a newsletter to update coalition members on activities.

Campaign information materials, including low literacy and Spanish-language adaptations, appropriate for distribution to each of the three target audiences were developed, e.g., fact sheets, magnets, flyers, door hangers, pins, posters, news alerts, stickers, slides, and postcards.

Assessment Data: The agreements signed by coalition members document the achievement of the target.

**Target 5: Ensure that no less than 85 percent of respondents to a customer feedback instrument rate NLM services at least satisfactory.**

Target significantly exceeded. A survey showed that 98% of users questioned rated NLM services as satisfactory or better, and 92% rated the services as good or excellent.

In June 2000, NLM conducted a survey of 565 customers using services available on-site at the library, requesting feedback on the specific use and service received. In answer to the question "Which best describes the general quality of service you received today?" 98.4% rated the service at least satisfactory, with 92% rating the service good or excellent.

Assessment Data: The June 2000 survey of 565 customers was OMB-approved.

**Target 6: Increase the usage of NLM's existing catalog-based databases for books, serials, and audiovisuals by 15%.**

Target significantly exceeded. FY 2000 usage of NLM's catalog-based databases increased by 27% over the FY 1999 level.

LOCATORplus, NLM's public access catalog, is available worldwide through the Internet, as well as on-site in the NLM Reading Room. In FY 2000, 538,080 searches were done on LOCATORplus, which is an average of 44,840 per month. This is a 27% increase over the FY 1999 usage level, which averaged 35,396 per month.

Assessment Data: These statistics are gathered monthly by NLM using the online documentation software package HTTP-ANALYZE 2.01. The NLM is now converting to a new software package called FunnelWeb Version 3, which will be the source of future statistics.

**Target 7: Increase the number of "health topics" in the Web-based MEDLINEplus to 300.**

Target significantly exceeded. MEDLINEplus contained 414 health topics as of the end of September 2000.

The information provided on each of the health topics is extensive and compiled from the NIH Institutes and other reliable sources. The selection and evaluation of material are done by experienced NLM medical librarians.

Assessment Data: MedlinePlus records. The alphabetical list of health topics may be accessed at <http://www.nlm.nih.gov/medlineplus/healthtopics.html>

***Progress Toward Goal Achievement***

Progress is being made to more fully inform the public about relevant research findings. NIH has accelerated efforts to communicate through the Internet, to form partnerships with other organizations, and establish a dialogue with the media. These efforts have expanded NIH's capacity to reach broader numbers of people. Because new findings will continue to emerge, it is likely that this will remain a goal of all NIH's Institutes well into the future.

***Next Steps***

Continued attention to this goal is needed and has been planned by NIH's Institutes. Ensuring that the public is informed and can take advantage of research advances is central to NIH's mission.

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

**Performance Targets & Results**

**FY 2002**

**Increase awareness of NIAMS-sponsored clinical research and generate interest in participating in clinical studies among minority populations.**

*Performance to be reported in February 2003.*

**FY 2001**

- 1. Educate the public about the importance of NIMH-supported clinical research and interest individuals and their families in participating in clinical studies.**
- 2. Increase the number of initial contacts about clinical trials with the Patient Recruitment and Public Liaison Office (PRPL).**
- 3. Improve NCI efforts to increase participation and retain minorities, under-served populations, and the elderly in clinical trials.**
- 4. Develop Web-based clinical trials tools that will improve the development, conduct, and ease of participation in NCI-sponsored clinical trials.**

*Performance to be reported in February 2002.*

**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.**

*Performance: Target substantially met. The Constituency Outreach and Education Program (COEP) was initiated in early 2000. COEP is a 5-year communications initiative of the NIMH that enlists State organizations in a nationwide partnership to help speed the translation of science into mental health services.*

- 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.**

*Performance: Target substantially met. NIMH has conducted focus groups with individuals from a variety of backgrounds, including representatives from racial and ethnic minority groups, to understand the motivations and barriers to participation in specific clinical trials.*

- 3. 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.**

*Performance: Target met. NCI developed a simplified and easy to understand informed consent form to help a patient understand a study's treatments and tests*

<b>Performance Targets &amp; Results</b>
<p><i>and its possible benefits and risks before he/she decides whether or not to participate.</i></p> <p>4. Increase visitors to NCI's cancerTrials Web Site 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.</p> <p><i>Performance: Target significantly exceeded. The total number of users has expanded by 33% and the range of information available on the Web site has been considerably enlarged.</i></p> <p><b>FY 1999</b></p> <p>Initiate a broad-based communications and public outreach program to reach physicians, and eventually, community groups and the general public.</p> <p><i>Performance: Target met. A broad-based communications and public outreach program was initiated in the 3rd quarter of FY 1999. This effort assisted NIH Institutes to accrue patients to clinical research studies by increasing awareness, prompting inquiries about research, and linking eligible patients to specific studies.</i></p>

Note: FY 2001 target #1 includes adjustments to the FY 2000 targets #1 and 2 activities that were incomplete at the end of the FY.

### ***Goal Background***

Increasing awareness and supporting participation in clinical trials has been identified as one of NIH's most critical communication challenges: To enable and support NIH-funded research, a steady, diverse, and substantial pool of patient and normal volunteers is needed. The quality of clinical research and its ability to improve the public's health care depend on the nation's physicians having the opportunity to refer patients to current studies and on patients having the information they need to learn about and participate in clinical trials.

### ***Performance Assessment Approach***

#### *Basis and Data:*

Outreach efforts will be tracked, documented, and assessed. Communication methods and materials will be evaluated to determine the reach to target audiences and the acceptance of the messages.

#### *Validation and Verification:*

Project implementation and impact findings will be confirmed in written documentation.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results*****Target 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.**

Target substantially met. The Constituency Outreach and Education Program (COEP) was initiated in early 2000. COEP is a 5-year communications initiative of the NIMH that enlists State organizations in a nationwide partnership to help speed the translation of science into mental health services. The program is a key element in a broader effort by NIMH to deliver science-based information on mental health to the public and health professionals and increase access to research-based, effective treatments.

Each Outreach Partner conducts a mental health communications program for the public and health professionals through media relations, statewide coalition building, and outreach to minorities and special populations such as youth and the elderly. Partners also sponsor educational efforts focusing on primary care physicians, nurses, employers, and other groups, and promote recruitment of participants in NIMH-supported clinical studies. Partners are invited to provide direct feedback to NIMH on its research priorities. NIMH provides Outreach Partners with ongoing technical assistance in project-related activities, research updates through annual meetings and the Web, opportunities to network on-line and in regional meetings with other State and national organizations, and educational materials.

The Institute has named Outreach Partners in 42 States and the District of Columbia and continues to seek Outreach Partners for the remaining 8 States and Puerto Rico. In addition, the program includes an Education Network of 200 mental health, medical, and business groups, whose State or regional affiliates engage in coalitions with the Outreach Partners.

Assessment Data: Information on activities and programs can be found on the COEP Web site at <http://www.outreach.nimh.nih.gov>.

**Target 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.**

Target substantially met. In an effort to understand the motivations and barriers to participation in specific clinical trials, NIMH has conducted focus groups with individuals from a variety of backgrounds including representatives from racial and ethnic minority groups.

NIMH conducted a series of twelve focus groups around the country (from New York to Portland OR) to specifically examine barriers to participation such as illiteracy, language, and age, as well as the concerns of minority and ethnic groups, and other hard-to-reach populations, and special issues that confront practitioners in reaching new immigrant groups in rural areas.



These focus groups have been conducted with patients and families, adult and minority mix, low literacy, illiterate and other first-spoken languages, depressed, and non-depressed teenagers, teenagers representative of the Latino, African American, and Asian populations, and with health practitioners in rural areas.

The next step is to take the data learned and develop messages and materials that will encourage these groups to consider participation in NIMH-sponsored clinical research studies.

Source of Assessment Data: The findings of the focus groups are documented in reports available from NIMH's Office of Communications and Public Liaison.

**Target 3: 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.**

Target met. The revised NCI clinical trial participant form template was developed and disseminated.

The National Cancer Institute, working with the Food and Drug Administration (FDA) and the Office for Protection from Research Risks (OPPR), developed, field-tested, and finalized guidelines for easy-to-understand informed consent documents along with a template document.

The template is now being disseminated more widely in the clinical trials community and has already been adopted by several other institutes and organizations. NCI also has developed a Spanish-language version of the template.

NCI is the recipient of a Creativity Award from the National Partnership for Reinventing Government for the revised consent form.

Assessment Data: Information about this activity can be found at <http://cancertrials.nci.nih.gov/understanding/indepth/protections/consent/pt01what.html>

**Target 4: Increase visitors to NCI's cancerTrials Web site 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.**

Target significantly exceeded. The number of visitors to the Web site and the amount of information made available has increased considerably.

Visitors to the cancerTrials Web site increased from about 15,000 users per week in 1999 to about 24,000 per week in 2000. The total number of users grew by about 200,000 -- a 33% expansion -- from the first year of operation (625,053 users over the period April 1998 to April 1999) to the second year (843,051 users over April 1999 to April 2000).

In addition, the information available on the Web site has expanded to cover prevention trials, such as STAR, cancer detection and diagnosis, such as colon cancer screening and biomedical imaging, and treatment for a wide variety of cancers. Also included are news and background information for patients, public, and the media and guides to resources for health professionals.

Assessment Data: Information available through the cancerTrials Web site, <http://cancertrials.nci.nih.gov>

### ***Progress Toward Goal Achievement***

Significant progress is being made to increase awareness of clinical research and support the participation in clinical trials. And in some cases, such as in the new Web site “clinicaltrials.gov,” progress has far surpassed expectations.

Considerable effort has been made to establish partnerships with national, regional, and local partners (voluntary organizations, professional groups) to increase awareness of research results and share information about relevant clinical studies, with a special emphasis toward reaching minority and ethnically diverse populations. In addition, there has been progress toward developing written materials that are easier to read and understand for English-speaking audiences as well as non-English speaking audiences. The Internet has also provided a rich opportunity to reach audiences with important clinical trials information.

### ***Next Steps***

Much of the groundwork has been laid to increase NIH’s capacity to help increase awareness of clinical research results and to help support participation in clinical trials. The efforts to increase awareness of clinical research in the area of mental health are still under way and are expected to be completed in FY 2001. There will be continued emphasis and expansion in this area as the initiatives described above move forward and reach their targets. There will be special efforts to reach ethnic groups and minority populations with relevant information.

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

**Performance Targets & Results**

**FY 2001**

1. **Promote the database as a resource for patients, physicians, researchers, community health groups and others.**
2. **Complete an implementation study to determine the optimal design and function of a toll-free telephone to facilitate access to the Clinical Trials Database.**
3. **Expand the number of industry-sponsored clinical trials in the database by 250 and the number sponsored by other federal agencies by 100.**

*Performance to be reported in February 2002.*

**FY 2000**

1. Expand the Clinical Trials Database to include trials from other federal agencies and the private sector.

*Performance: Target met. The Clinical Trials Database became available to the public on February 29, 2000. At the end of FY 2000, 800 of the more than 5,000 trials included in the database were trials supported by the private sector or other federal agencies.*

2. Develop options for implementation of toll-free telephone access to information in the Clinical Trials Database.

*Performance: Target substantially met. NIH has procured the services of an outside contractor to conduct an implementation study pertaining to the toll-free telephone access. An initial summary report, including possible implementation strategies, was received soon after the close of FY 2000. A final report is near completion.*

**FY 1999**

Develop and implement the Clinical Trials Database.

*Performance: Target met. Data elements were developed for the Clinical Trials Database based on the legislative requirements and discussions with collaborating NIH Institutes and Centers (ICs) and other group. A prototype Internet-based database was designed and an on-line data entry system developed for use by NIH ICs. Data from the eight existing clinical trials databases together with data from all other ICs that support clinical trials were incorporated into the prototype system. In addition, focused testing was conducted.*

Note: Completion of this goal is expected in FY 2001.

### ***Goal Background***

Currently, there is no consolidated source of information on clinical trials for drugs for serious or life threatening diseases and conditions. 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. Facilitating access to information on clinical trials is an important national goal. At the present time, the NIH Home Page provides consolidated access to eight clinical trials databases: the NCI's Physician's Data Query; the AIDS Clinical Trials information System, Rare Disease Clinical Trials Database; Clinical Center Studies, the NEI Clinical Trials database, the NHLBI Clinical Trials database, the NIA Alzheimer's Disease Clinical Trials database, and the NIAID Clinical Trials database. A central or common database does not exist. The database required by the FDA Modernization Act will include all federally and privately funded clinical trials for drugs for serious or life threatening diseases and conditions submitted under Investigational New Drug (IND) applications.

Establishing toll-free telephone access to the Clinical Trials Database will be complex and expensive. Due to the uncertainties regarding the demands that could be placed upon the system (that is, the number of calls), the many possible designs for the system, and the varying levels of service that might be provided, a competitive contract will be awarded to study options for design and level of service.

Nevertheless, improving access to clinical trial information addresses head-on one of NIH's most critical challenges—increasing public and provider awareness, understanding, and willingness to participate in clinical research (clinical trials).

### ***Performance Assessment Approach***

#### *Basis and Data:*

The principal measures of achievement for each of these targets are implementing the projects and subsequently tracking, documenting and assessing the effects of outreach and informational activities.

#### *Validation and Verification:*

Achievement of these targets will be documented in publicly accessible reports.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target 1: Expand the Clinical Trials Database to include trials from other federal agencies and the private sector.**

Target met. The Clinical Trials Database became available to the public on February 29, 2000, <http://clinicaltrials.gov>. At the end of FY 2000, 800 of the more than 5,000 trials included in the database were trials supported by the private sector or other federal agencies.

At launch, the database contained approximately 4,000 trials, about 400 of which were supported by industry or other federal agencies. As of September 30, 2000, the database had increased in size by 25 percent, containing more than 5,000 clinical trials at more than 47,000 locations nationwide.

Over the same period the number of non-NIH supported trials doubled, to about 800. These are primarily in the areas of cancer and HIV/AIDS trials. About 700 are industry supported; 100 are supported by other federal agencies.

Nonetheless, there is more work to be done. The Food and Drug Administration estimates there are some 2,300 new industry protocols each year that require submission to Clinicaltrials.gov. In FY 2001, the FDA is implementing a pilot project with 25 volunteer companies who will each submit 10 protocols for the database.

Assessment Data: The information is available from the Clinical Trials Database at <http://clinicaltrials.gov>.

## **Target 2: Develop options for implementation of toll-free telephone access to information in the Clinical Trials Database.**

Target substantially met. NIH has procured the services of an outside contractor to conduct an implementation study regarding the creation of the toll-free telephone communications service for disseminating clinical trials database information. (The toll-free telephone service will complement the Clinical Trials Database – [www.clinicaltrials.gov](http://www.clinicaltrials.gov)) Soon after the close of FY 2000, NIH received an initial summary report from the contractor, including possible implementation strategies. Presently, the final report is near completion.

The purpose of the study is to: define the primary operating strategies for the service, map the associated operating characteristics and costs, and explore potential options for enhancing the nature of the base service offered.

During FY 2000, the following tasks were completed: a review of the literature regarding health-related telephone services; focus groups of potential users (reports were submitted to the NIH), and a series of interviews with NIH communications staff whose operations would be affected by the telephone service; and a series of interviews with health care providers (who may use the service).

Assessment Data: The Request-for-Quotation (RFQ) seeking contractor support to conduct the implementation study is on file in NIH Contracts. Focus group reports (with potential users of the service), a literature review of existing telephone services, and reports of interviews with

NIH communication staff and health professionals are available from the NIH Office of Communications and Public Liaison.

***Progress Toward Goal Achievement***

A database containing NIH clinical trials has been designed, developed, tested, and implemented. The initial public database (opened to the public in February 2000) contained about 4,000 clinical trials. By the end of the FY 2000, the database contained slightly more than 5,000 trials.

***Next Steps***

The emphasis in FY 2001 will be to include more non-NIH sponsored trials -- largely from American pharmaceutical firms. NIH is working closely with the FDA and other federal agencies to have their trials submitted to the Clinical Trials Database. In addition, NIH is working with the FDA to develop a final Guidance Document (including an implementation plan) to facilitate inclusion of non-NIH sponsored trials in the database.

Once the toll-free telephone service implementation study is completed, NIH will use the results to determine the optimal design for the telephone service, develop a Request-for-Proposals, and begin the procurement process to secure the services of a contractor to operate the telephone service under the supervision of the NIH.

### 2.1.2.3 Technology Transfer

The broad purpose of NIH's technology transfer activities is to promote the efficient transfer of new technology forthcoming from NIH research to the private sector, to facilitate and enhance the development of new drugs, other products, and methods of treatment that benefit human health. Beyond the promise to advance public health, technology transfer contributes to the global competitiveness of the nation's businesses and ultimately to the U.S.'s economic prosperity.

At present, NIH has one of the most active technology transfer programs in government. Through these activities, NIH has forged partnerships with industry and other external research organizations that have enhanced and augmented the capacity of NIH to conduct laboratory and clinical research.

To achieve the potential, NIH must continue to build the organizational structure necessary to facilitate technology transfer for NIH-supported investigators, develop effective, well-articulated technology transfer policies, guidelines and procedures and monitor licensee activities. This will involve:

- Working with the Department of Health and Human Services, the Congress, and our research partners to establish and implement rational technology transfer policies.
- Establishing timely and effective procedures and guidelines that facilitate patenting, licensing, and cooperative research projects within intramural NIH;
- Encourage and provide incentives for NIH intramural scientists to participate in technology transfer.
- Encourage the transfer of technology to develop new products to improve public health.

The following performance goals address key aspects of these areas.

**Performance Goals Summary Table – Technology Transfer**

Performance Goals	FY Targets	Actual Performance	Details
<p><b>a) Increase the number of scientists who have received training in technology transfer.</b></p>	<p><b>FY 2002</b> Seek to increase the percentage to 33% the number of scientists who complete the Web based training module and/or attend technology transfer seminars.</p> <p><b>FY 2001</b> Seek to have 15% of scientists complete the training module, and/or attend technology transfer seminars.</p> <p><b>FY 2000</b> 1. Implement training module.</p> <p>2. Contact 20% of NIH scientific staff.</p> <p><b>FY 1999</b> Contractor development of a Web-based training module.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially met. The training model was completed in FY 2000 and then activated on the Web in the first month of FY 2001.</p> <p>Target not met. Training activities were not commenced due to training module software development delays.</p> <p><b>FY 1999</b> Target not met. Although, there was progress in the development of the training module.</p>	<p>Page 191</p>
<p><b>b) Enhance outreach to commercial entities.</b></p>	<p><b>FY 2000</b> 1. Increase in the number of EIRs by 5% or more over the FY 1999 level.</p> <p>2. Increase the number of License Agreements executed in FY 2000 by 3% over the FY 1999 level.</p> <p>3. Increase the number of executed CRADAs by 3% over the level in FY 1999.</p> <p><b>FY 1999</b> 1. Increase the number of EIRs by 5% or more over the FY 1998 level of 287.</p> <p>2. Increase the number of license agreements executed in FY 1999 by 3% over the 215 executed in FY 1998.</p>	<p><b>FY 2000</b> Target significantly exceeded. 330 EIRs, an increase of 12% over the FY 1999 level.</p> <p>Target not met. 188 license agreements executed, a decrease of 8%.</p> <p>Target not met. 34 new CRADA agreements, a decrease of 14%.</p> <p><b>FY 1999</b> Target not met. 294 EIRs, an increase of 2.5% over the FY 1998 level.</p> <p>Target not met. 204 license agreements executed, a 5% decrease.</p>	<p>Page 194</p>



Performance Goals	FY Targets	Actual Performance	Details
	<ol style="list-style-type: none"> <li>3. Increase the number of executed CRADAs by 3% over the 43 executed in FY 1998.</li> </ol>	<p>Target significantly exceeded. 48 CRADAs executed, an increase of 10%.</p>	
<p><b>c) Develop a system to identify and measure the health outcomes of technologies licensed by the NIH</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Develop two case studies to test the proposed methodology.</li> <li>2. Finalize the approach.</li> <li>3. Apply the methodology to 10% of all exclusively licensed technologies which are a part of commercially available products.</li> </ol> <p><b>FY 2001</b></p> <p>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.</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p>	<p>Page 198</p>
<p><b>d) Maintain oversight and protection of the public investment in NIH research through increased monitoring of licensee activities.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Continue to reduce delinquencies over 180 days and bring that number to zero by the end of FY 2002, except for cases which are being actively negotiated due to the affect on public health.</li> <li>2. Establish procedures to ensure that all delinquent payments associated with terminated licenses will be submitted to the NIH Debt Collection Officer within 120 days of termination.</li> <li>3. Continue to perform audits on up to 3 licensees during the year, if warranted.</li> <li>4. Implement a data system which includes all license monitoring milestones and benchmarks for all exclusive licenses.</li> </ol> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Reduce the number of delinquent payments over 180 days by 50% from the number in place at the end of FY 2000.</li> <li>2. Reduce the number of terminated licensees with outstanding royalty</li> </ol>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p>	<p>Page 200</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>amounts owed by 10% from the number at the end of FY 2000.</p> <ol style="list-style-type: none"> <li>3. 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.</li> <li>4. When indicators show that sales and royalty information may be incorrect, conduct audits of up to 3 licensees during the year.</li> <li>5. Recruit and select personnel to establish a special license monitoring unit to provide oversight of licensee progress in developing and commercializing technologies licensed from the NIH.</li> </ol>		
<p><b>e) Patent portfolio review and management to maximize return for public health.</b></p>	<p><b>FY 2000</b> No more than 30% of unlicensed patents from before FY 1995 being retained by the agency.</p> <p><b>FY 1999</b> No more than 50% of unlicensed patents from before FY 1995 being retained by the agency.</p>	<p><b>FY 2000</b> Target met. The number of unlicensed patents has been reduced to 28.5%.</p> <p><b>FY 1999</b> Target met.</p>	<p>Page 202</p>

**Performance Goal Details - Technology Transfer**

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

**Performance Targets & Results****FY 2002**

**Seek to increase the percentage to 33% the number of scientists who complete the Web based training module and/or attend technology transfer seminars.**

*Performance to be reported in February 2003.*

**FY 2001**

**Seek to have 15% of scientists complete the training module, and/or attend technology transfer seminars.**

*Performance to be reported in February 2002.*

**FY 2000**

1. Implement the training module.

*Performance: Target substantially met. Development of the training module was completed in FY 2000 and then activated on the Web in the first month of FY2001 (October 2000).*

2. Contact 20% of NIH scientific staff.

*Performance: Target not met. Due to software development delays, it was not possible to commence training activities in FY 2000.*

**FY 1999**

Contractor development of a Web-based training module.

*Performance. Target not met. Progress was made in the contractor's development of the training module. But there was a delay in the scripting of some components.*

Notes: Due to the FY 1999 delay reported above, development of the training module continued into FY 2000. Accordingly, the planned FY 2000 implementation of the module (target #1) will not be completed until FY 2001.

**Goal Background**

It is important that NIH's scientific and technology transfer staff have up-to-date information on legal requirements, policies, and procedures regarding technology transfer activities and

responsibilities as a federal employee. The broad purpose of this goal is to provide information and training to the scientific community at NIH on technology transfer procedures.

As of FY 1999, there are approximately 4,000 research investigators who would be targets for such training. This goal is a continuing activity, based on training efforts developed in FY 1999 and FY 2000.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

FY 2002 -- A key measure is the number of scientists completing the online web training. The target also includes attendance at technology transfer seminars at individual Institutes, as well as those across the NIH.

FY 2001 -- Several measures provide a comprehensive account of progress in achieving this goal's targets -- attendance of NIH scientists at the Annual Technology Transfer Retreat and related seminars, distribution of policies and information materials, and the number of scientists who access and complete the new on-line Web-based training module.

#### ***Validation and Verification:***

Seminar attendance sheets and information available from the new Web-based training program will provide objective data on the extent of participation.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

#### **Target 1: Implement training module**

Target substantially met. Development of the training module was completed in FY 2000 and then activated on the Web in October 2000.

The module has been broadly tested. The scientists participating in this process have been pleased with the module's content and ease of use.

Assessment Data: The training module can be viewed at <http://137.187.172.30/cbttng/default.asp?cbtid=1>

#### **Target 2: Contact 20% of the NIH scientific staff**

Target not met. Due to the longer time needed to finalize the training module, no formal training was conducted in FY 2000.

***Progress Toward Goal Achievement***

Considerable progress toward the goal has been made with the actual activation of the new training module.

With this accomplishment, the thrust of the effort turns toward encouraging NIH scientists to engage the training resources the module now provides.

***Next Steps***

Institute Scientific Directors will be asked to encourage their scientists to access the training module.

**Goal b) Enhance outreach to commercial entities.****Performance Targets & Results****FY 2000**

1. Increase the number of EIRs by 5% or more over the FY 1999 level.

*Performance: Target significantly exceeded. There were 330 EIRs in FY 2000, a 12% increase over the FY 1999 figure.*

2. Increase the number of License Agreements executed in FY 2000 by 3% over the FY 1999 level.

*Performance: Target not met. 188 License Agreements were executed in FY 2000, a decrease of 8% compared to the FY 1999 level.*

3. Increase the number of executed CRADAs by 3% over the level in FY 1999.

*Performance: Target not met. 34 new CRADA agreements were established in FY 2000, a decrease of 14% compared to the FY 1999 level.*

**FY 1999**

1. Increase the number of EIRs by 5% or more over the FY 1998 level of 287.

*Performance. Target not met. There were 294 EIRs in FY 1999, a 2.5% increase over the FY 1998 level.*

2. Increase the number of license agreements executed in FY 1999 by 3% over the 215 executed in FY 1998.

*Performance. Target not met. 204 agreements were executed in FY 1999, a 5% decrease over the FY 1998 level.*

3. Increase the number of executed CRADAs by 3% over the 43 executed in FY 1998.

*Performance. Target significantly exceeded. 48 CRADAs were executed in FY 1999, a 10% increase over the FY 1998 level.*

Notes: This goal will not tracked for GPRA purposes beyond FY 2000. Goal c) (described subsequently) is being introduced in FY 2001 as a replacement, to better measure the outcomes of principal management interest. Nevertheless, data for the activity measures above will continue to be submitted annually, through the Dept. of Commerce, under terms of the Technology Transfer Commercialization Act of 2000.

**Goal Background**

This goal involves technology transfer activities along a number of lines: enhance NIH marketing with commercial entities; improve electronic and other marketing techniques to simplify access to NIH technologies for licensing purposes; improve the search engine for use in

reviewing NIH technologies available for licensing; and work with NIH's Institutes and the private sector to promote industry participation and investment in research.

Several measures have been viewed as metrics for gauging the overall success of these efforts:

Employee Invention Reports (EIRs) -- In the technology transfer field, a general "rule of thumb" has evolved over time which estimates the level of invention reporting that can reasonably be anticipated from research activity. NIH's goal is to eventually reach the "rule of thumb" ratio of one EIR per \$2 million of intramural research funding. Without technologies constantly being developed and in the pipeline, a technology transfer program cannot survive.

Licensing Agreements -- To increase productivity and the movement of technologies from the laboratory into the marketplace, NIH proposes to increase activity associated with marketing and licensing of available technologies, with a goal of increasing the number of licensing agreements by 3% over the corresponding figure for the previous fiscal year.

Cooperative Research and Development Agreements (CRADAs) -- The agency uses the CRADA mechanism to enable commercial entities to work with federal laboratory personnel in collaborative activities to enhance possible development of new technologies that would be difficult to develop in isolation. This goal is to continue at 3% per annum growth rate for the foreseeable future.

It should be noted, however, that increased activity in each of these areas is challenging to develop and subject to numerous external influences that could diminish year-to-year increases. These factors include, among others, the shifting of research interests by possible partners, the continuing desirability of working as a partner with the federal government and adhering to government requirements, internal staffing levels and resources, and economic conditions affecting private industry.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

All data will be taken from the NIH Office of Technology Transfer's (OTT) Invention Tracking System. This database contains NIH's official information on each reported technology transfer activity.

#### ***Validation and Verification:***

The Invention Tracking System database is updated daily. It provides a reliable account of invention reports and agreements at NIH.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results*****Target 1: Increase in the number of EIRs by 5% or more over the FY 1999 level.**

Target significantly exceeded. The number of EIRs increased by 12% over the FY 1999 level (330 in FY 2000 vs. 294 in FY 1999).

**Target 2: Increase the number of License Agreements executed in FY2000 by 3% over the FY1999 level.**

Target not met. The number of License Agreements executed decreased by 8% compared to FY 1999 (188 in FY 2000, down from 204 in FY 1999). This result is primarily a consequence of NIH licensing staff turnover and vacancies during FY 2000.

**Target 3: Increase the number of executed CRADAs by 3% over the level in FY 1999.**

Target not met. CRADA activity decreased by 14% compared to FY 1999 (34 in FY 2000, down from 48 in FY 1999). NIH Institutes, which enter into these agreements, believe this result may indicate that NIH is approaching a saturation point for CRADA partnerships. At the end of FY 2000, the NIH has over 190 active standard CRADA partnerships.

Assessment Data: The data cited comes from the NIH Invention Tracking System. (See the *Performance Assessment Approach* section above for a further discussion.)

***Progress Toward Goal Achievement***

These measures have proved to be unsatisfactory in gauging the success of technology transfer program performance. To a large extent, the presence of many of the “external influences” identified in the *Background* discussion in the observed outcomes have made it difficult to separate the effects of NIH management from the influence of uncontrolled, outside factors.

Accordingly, OTT has determined that new performance measures need to be developed, that can better track the downstream social and economic impacts of the technologies developed through NIH scientists’ activities that are brought to the market by licensees.

In keeping with this, the Goal b) activity measures will not be tracked beyond FY 2000. In FY 2001 and beyond, Goal b) will be replaced by the performance assessment approach embodied in Goal c).



It should be noted, however, that data for the three Goal b) measures will continue to be reported annually to the Congress through another venue, as specified by the Technology Transfer Commercialization Act of 2000 (P.L. 106-404).

*Next Steps*

See the discussion for Goal c).

<b>Goal c)      Develop a system to identify and measure the health outcomes of technologies licensed by the NIH</b>
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<b>Performance Targets &amp; Results</b>
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<b>FY 2002</b>
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|--|
| <ol style="list-style-type: none"> <li>1. <b>Develop two case studies to test the proposed methodology.</b></li> <li>2. <b>Finalize the approach.</b></li> <li>3. <b>Apply the methodology to 10% of all exclusively licensed technologies which are a part of commercially available products.</b></li> </ol> |
|--|

<p style="text-align: center;"><i>Performance to be reported in February 2003.</i></p>
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<b>FY 2001</b>
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<p><b>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.</b></p>
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<p style="text-align: center;"><i>Performance to be reported in February 2002.</i></p>
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Notes: This is a new goal in FY 2001. It replaces Goal b), with the intent of better measuring key outcomes of management interest.

### ***Goal Background***

The value and effect of NIH activities in technology transfer activities requires the development of new performance measures. The program believes that we need to develop measures of the social and economic downstream effect of technologies developed through NIH scientists' activities that are brought to the market by licensees.

Potential measures include: dosages prescribed or used, reduction in mortality/morbidity, reduction in number of sick days used, extension of life, etc. These are quite complex issues that involve numerous factors which must be carefully defined and analyzed.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

Performance will be assessed according to the target milestones specified above. The measurement approach will be based on publicly available data and reports.

*Validation and Verification:*

Documentation on file will confirm the findings, recommendations, and achievements forthcoming from these tasks.

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

### Performance Targets & Results

#### FY 2002

1. Continue to reduce delinquencies over 180 days and bring that number to zero by the end of FY 2002, except for cases which are being actively negotiated due to the affect on public health.
2. Establish procedures to ensure that all delinquent payments associated with terminated licenses will be submitted to the NIH Debt Collection Officer within 120 days of termination.
3. Continue to perform audits on up to 3 licensees during the year, if warranted.
4. Implement a data system which includes all license monitoring milestones and benchmarks for all exclusive licenses.

*Performance to be reported in February 2003.*

#### FY 2001

1. Reduce the number of delinquent payments over 180 days by 50% from the number in place at the end of FY 2000.
2. Reduce the number of terminated licensees with outstanding royalty amounts owed by 10% from the number at the end of FY 2000.
3. 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.
4. When indicators show that sales and royalty information may be incorrect, conduct audits of up to 3 licensees during the year.
5. Recruit and select personnel to establish a special license monitoring unit to provide oversight of licensee progress in developing and commercializing technologies licensed from the NIH.

*Performance to be reported in February 2002.*

Note: This is a new goal in FY 2001.

#### ***Goal Background***

While the transfer of technology is an important concern, it is equally important to ensure that the licenses of technologies to commercial entities are being implemented properly and the

amount of royalties being paid to the government correct. In support of this concern the Office of Technology Transfer (OTT) is implementing a new monitoring strategy for NIH technologies that are licensed. The monitoring effort is a three pronged approach to (1) maintain oversight of licensee activities and progress toward development and commercialization of licensed technologies, (2) ensure that royalties owed to the government are made in a timely and appropriate manner, including, as necessary, the auditing of licensees and (3) pursue licensing of technologies to entities who are infringing on NIH intellectual property.

***Performance Assessment Approach***

*Basis and Data:*

Performance will be assessed according to the target milestones specified above. The necessary information will be drawn from OTT data systems, audits, written procedures, and personnel actions.

*Validation and Verification:*

Copies of all documents pertinent to the conduct of this goal are kept on file at OTT.

<b>Goal e)      Patent portfolio review and management to maximize return for public health.</b>
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Performance Targets & Results
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<b>FY 2000</b>
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No more than 30% of unlicensed patents from before FY 1995 being retained by the agency.
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<i>Performance:</i> Target met. The number of unlicensed patents has been reduced to 28.5%
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<b>FY 1999</b>
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No more than 50% of unlicensed patents from before FY 1995 being retained by the agency.
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<i>Performance.</i> Target met.
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Note: This goal has been completed in FY 2000 and will not be further tracked for GPRA purposes.

### ***Goal Background and Significance***

The agency needs to monitor its portfolio of patented technology to ensure that time and resources are not being spent on technologies which are outdated because of new inventions or new avenues of research have rendered the technology to be of little commercial value. The agency will undertake reviews with intramural laboratory staff to delete these types of technologies from our patent portfolio and retain an inventory of technologies that have utility and can be actively marketed. A sound management target which is based on professional technology transfer staff judgments, is that the inventory will include no more than 30% of the pre FY1995 unlicensed patents as of the onset of this initiative.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

The percentage of pre-FY 1995 patents remaining in the current portfolio unlicensed provides a direct measure of the progress on this goal. An assessment of the FY1999 and FY 2000 patent license portfolio will be conducted to determine this figure. Data for this portfolio review will be generated from NIH's new Technology Transfer Information Management System. (TTIMS).

#### ***Validation/Verification:***

The TTIMS is an integrated information system used in day to day operations of OTT. Data is drawn from the day-to-day activities and is collected in specially designed reports. Data

integrity is important for all aspects of operations and continual checks are made on the veracity of the data.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: No more than 30% of unlicensed patents from before FY 1995 being retained by the agency.**

Target met. Portfolio reviews by OTT and Institute personnel have led to the reduction of unlicensed patents to 32.5% of the entire portfolio. However, analysis found that approximately 4% of the patents had made their final US annuity payments and may be held available for licensing to the full extent of their patent term without incurring any further cost to the government. And with deduction of this 4% of patents, the ratio is reduced to 28.5%, thus the intent of the goal of reducing unlicensed patents to no more than 30% has been met.

Assessment Data: The data reported come from OTT's Invention Tracking System.

#### ***Progress Toward Goal Achievement***

The FY 2000 progress has been sufficient to complete this goal. Accordingly, it will not be further tracked for GPRA purposes.

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### 2.1.2.4 Research Leadership and Administration

Setting research priorities, encouraging scientific innovation, determining which scientific projects and scientists receive funding, and efficiently using the resources available to support medical research are essential catalysts for progress in medicine and health care. NIH views its leadership in these realms as an important stewardship for the nation's medical research enterprise.

Achieving these purposes depends on effective NIH action in several critical scientific, management, and administrative areas. These include:

*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.

Each of these areas is discussed more fully below and is the subject of performance goals pertaining to the operations involved or ongoing improvements in process capabilities.

#### Priority Setting

Priority setting is a complex activity; many decisions must be made during the complex process of deciding how the NIH will spend its money. This process occurs at many levels within the Administration—and the Congress must then ultimately determine, with the President's agreement—how much money to provide to each IC.

Many criteria guide the development and expenditure of the NIH budget, including: (1) an obligation to respond to public health needs; (2) a commitment to support work 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 insure a strong scientific infrastructure, with a high quality workforce and excellent research facilities.

Congress, the public, health advocacy groups, and researchers have had a long-standing interest in priority setting at the NIH. This interest was reflected, in part 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 has effectively responded to, the recommendations made by the IOM.

The agency continues to engage the public in a variety of activities related to priority setting. Opinions are solicited from, and provided by, many groups and individuals—the extramural scientific community, patient advocacy groups, Congress and the Administration, and the NIH staff. We gather these opinions through many means, as appropriate to the decision-making process. For example:

- NIH convenes review groups composed of accomplished investigators to evaluate grant applications for scientific merit;
- each IC convenes meetings of national advisory councils, with members from the public, medical, and scientific communities, to review a broad range of IC policies;
- many conferences, workshops, and studies are organized or commissioned each year to gather opinions on specific scientific, health, ethical, and administrative issues;
- the ICs have highly evolved processes for reviewing scientific progress in their areas of responsibility, for developing long-range research objectives, and for formulating annual budgetary plans and research initiatives;
- the NIH has made frequent use of extramural advisory groups to assess trans-NIH activities and to recommend budgetary and programmatic changes in those areas; and the IC Directors; and
- NIH staff consult with members of other Federal agencies, the OMB and DHHS, Congressional members and staff, and professional and health advocacy organizations for guidance on a variety of common concerns.

The collective views of the aforementioned individuals and groups inform us about emerging public health needs and scientific opportunities. The results of these efforts are incorporated into plans, and ultimately the decisions, the NIH makes about resource allocation for biomedical research.

## **Grants Administration and Peer Review**

Approximately eighty-five percent of NIH's budget goes to support research in universities, medical centers, and other institutions around the country. As such, NIH considers it very important to maintain effective and efficient grants administration and a high quality of peer review, such that the highest quality of research is selected for support.

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, provide advice to NIH staff in the selection process. After NIH awards funds, it ensures that the research is carried out appropriately.

The most important requirements of the peer review process are that the process is fair, remains current with the science it is reviewing, and is organizationally well designed to accommodate the many applications for research support and training that NIH receives. It is also essential that

NIH provide support to investigators in a timely fashion, so that the important effort of providing for the health of the nation can proceed efficiently.

Finally, the expenditure of the nation's financial resources for the conduct of research also demands appropriate oversight. And towards this end, efficient and effective administration, improved customer service, and enhanced communication and reporting processes are essential.

Maintaining the effectiveness of the numerous processes and systems involved and responding to the evolving needs of science are continuing efforts. The areas below reflect current priorities, and form the basis for the performance goals discussed in the subsequent pages of this section:

- Improve the support for research by reviewing current mechanisms and implementing appropriate changes
- Improve the responsiveness and efficiency of NIH's research administration systems to the grantee community
- Strengthen NIH's capacities for the conduct of electronic research administration
- Strengthen grantee institution compliance with grant requirements
- Ensure that grant applications submitted to NIH receive fair and appropriate review.

### **Agency Management and Administrative Support**

NIH would be unable to maintain its world-class stature in research without strong management and administrative and management support to the research community. These support services are provided centrally at NIH.

These support services include: (1) advising the NIH Director and staff on all phases of NIH-wide administration and management activities; (2) providing leadership and direction to all aspects of management; (3) overseeing the management of functions in the area of 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.

The major concerns currently in the management and administration realm are:

- Ensuring that NIH makes its information technology investments in ways that support the overall NIH Mission
- Improving efficiency and effectiveness for all procurement and contracting activities

**Performance Goals Summary Table – Research Leadership and Administration**

Performance Goals	FY Targets	Actual Performance	Details
<p><b>• PRIORITY SETTING</b></p>			
<p><b>a) Ensure that NIH-supported research reflects the changing nature of scientific opportunities and public health needs.</b></p>	<p><b>Annual Target</b> Sponsorship of Institute and Center workshops and panels that assess scientific progress and identify emerging public health needs and scientific opportunities. Incorporate the findings and recommendations from these workshops and panels into updated and/or new plans, priorities, and proposal submission requests for Institute and Center research programs.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target met. Numerous workshops and other meetings were convened that resulted in new programmatic initiatives.</p> <p><b>FY 1999</b> Target met. Numerous workshops and other meetings were convened that resulted in new programmatic initiatives.</p>	<p>Page 215</p>
<p><b>b) Progress in responding to the Institute of Medicine Report recommendations for improving public input and priority setting at the NIH.</b></p>	<p><b>FY 2000</b> Development of draft strategic plans by each of the research Institutes and Centers.</p> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Implementation of activities to enhance public input into NIH activities.</li> <li>2. Progress in implementing appropriate recommendations of the Institute of Medicine regarding the NIH priority setting process.</li> </ol>	<p><b>FY 2000</b> Target Met. Each of NIH’s Institutes and Centers has developed a strategic plan.</p> <p><b>FY 1999</b> Target met. Office of Public Liaison in Office of Director Established. Director’s Council of Public Representatives established. Other initiatives taken.</p> <p>Target met. NIH took actions responding to all 12 of the IOM’s recommendations in its July 1998 report.</p>	<p>Page 228</p>
<p><b>• GRANTS ADMINISTRATION AND PEER REVIEW</b></p>			
<p><b>a) Ensure proper stewardship of public funding for research.</b></p>	<p><b>FY 2002</b> Publish a report of findings, lessons learned, and best practices observed in the conduct and administration of sponsored programs at NIH’s recipient institutions.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p>	<p>Page 231</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Create an organizational component within NIH with FTE's devoted expressly to compliance-related activities.</li> <li>2. Perform a minimum of 10 compliance site visits.</li> </ol>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p>	
<p><b>b) 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.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Complete Formation of all external IRG Working Groups.</li> <li>2. Increase number of Steering Committees and Study Section Boundaries teams from 4 to 10.</li> </ol> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Increase the number of IRG external advisory groups from 8 to 14.</li> <li>2. Create 4 Steering Committees and their respective SSB teams.</li> </ol> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>1. Enhance study section operations by doubling the number of IRG external advisory groups from 3 to 6.</li> <li>2. Complete Phase 1 of Panel on Scientific Boundaries for Review and develop an Implementation Plan for Phase 2.</li> </ol> <p><b>FY 1999</b> Conduct various assessments of the functions and organization of NIH study sections.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target significantly exceeded. Ten external working groups formed.</p> <p>Target met. Phase 1 final report completed and Phase 2 implementation initiated.</p> <p><b>FY 1999</b> Target met. Assessments completed.</p>	<p>Page 233</p>
<p><b>c) Improve Electronic Research Administration (ERA) technology and enhance communication with the extramural community.</b></p>	<p><b>FY 2002</b> Integrate the NIH Commons with the Federal Commons.</p> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Implement electronic progress reporting with all 65 newly on-line institutions participating in the FDP.</li> <li>2. Begin pilot testing of progress reporting for multi-project mechanisms.</li> </ol>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p>	<p>Page 237</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>1. Full deployment of key ERA business process modules.</li> <li>2. Implement electronic progress reporting with all 65 newly “on-line” institutions participating in the FDP.</li> <li>3. Begin pilot testing of progress reporting for multi-project mechanisms.</li> </ol> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Design and test new systems.</li> <li>2. Streamline post-award reporting, while continuing to ensure appropriate oversight and enhancement of recipient compliance with reporting and accountability requirements.</li> </ol>	<p><b>FY 2000</b></p> <p>Target met. Key business process models in NIH Commons made widely available.</p> <p>Target not met. Only limited progress achieved.</p> <p>Target not met. No new development in FY 2000.</p> <p><b>FY 1999</b></p> <p>Target met. The Electronic Notice of Grant Award (NGA) system was pilot tested in FY 1998 and fully deployed at the beginning of FY 1999</p> <p>Target met. E-SNAP began receiving the first electronic applications in a limited pilot in May 1999.</p>	
<p><b>d) Develop innovative business practices to facilitate government/public interactions.</b></p>	<p><b>FY 2002</b></p> <p>Pilot test ways to further simplify SNAP.</p> <p><b>FY 2001</b></p> <p>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.</p> <p><b>FY 2000</b></p> <p>Expedite the processing of the most meritorious grant applications by extending to all NIH Institutes the use of expedited en bloc Council review procedures.</p> <p><b>FY 1999</b></p> <p>Identify approaches to expedite the processing and award of grant applications.</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p> <p><b>FY 2000</b></p> <p>Target met. Policy announcement encourages adoption of and provides guidance for expedited procedures.</p> <p><b>FY 1999</b></p> <p>Target met. Procedures established to significantly expedite the awards process.</p>	<p>Page 242</p>

Performance Goals	FY Targets	Actual Performance	Details
<p><b>e) Improve grantee reporting of inventions developed with federal funds.</b></p>	<p><b>FY 2002</b> Integrate Edison into the Federal Commons (a governmental electronic grants and contracts administration system).</p> <p><b>FY 2001</b> 1. Identify ways to improve historical invention reporting data. 2. Further educate constituents of their invention reporting obligations.</p> <p><b>FY 2000</b> Fully establish the Edison electronic invention reporting system for use by all grantee institutions, and expand its use to other government agencies.</p> <p><b>FY 1999</b> Enhance recipient compliance with reporting and accountability requirements.</p>	<p><b>FY 2000</b> Target met. The Edison system is capable of being used by all grantee institutions.</p> <p><b>FY 1999</b> Target met. 189 grantee institutions using Edison (40% increase over 1998 level). Memoranda of Understanding with several federal agencies for use.</p>	<p>Page 245</p>
<p><b>• AGENCY MANAGEMENT AND ADMINISTRATIVE SUPPORT</b></p>			
<p><b>a) Implement the recommendations of the Arthur Andersen, Inc. study of administrative practices and costs at NIH.</b></p>	<p><b>FY 2001</b> Finish meeting the milestones and targets that go beyond the FY 2000 goals.</p> <p><b>FY 2000</b> Complete the implementation of all recommendations as decided upon by the NIH Director and the IC Directors.</p> <p><b>FY 1999</b> 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.</p>	<p><b>FY 2001</b> To be reported in 2002.</p> <p><b>FY 2000</b> Target substantially met. 70 of 76 NIH-elected recommendations have been implemented.</p> <p><b>FY 1999</b> Target met. NIH elects to implement 76 of 80 Anderson recommendations  Target met. CFO and CIO recommendations implemented.</p>	<p>Page 248</p>

Performance Goals	FY Targets	Actual Performance	Details
<p><b>b) Improve the efficiency of the small acquisition process by continuing to expand the Purchase Card Program.</b></p>	<p><b>FY 2002</b> \$220 million in orders.</p> <p><b>FY 2001</b> \$200 million in orders.</p> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>1. \$160 million in orders.</li> <li>2. 3,600 people trained to use cards.</li> <li>3. 2,000 card holders.</li> </ol> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. \$110 million in orders.</li> <li>2. 3,000 people trained to use cards.</li> <li>3. 1,600 card holders.</li> </ol>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target met. \$173 million in orders.</p> <p>Target substantially met. 3,391 persons trained.</p> <p>Target substantially met. 1,729 cardholders.</p> <p><b>FY 1999</b> Target met. \$130 million in orders</p> <p>Target substantially met. 2,860 people trained</p> <p>Target substantially met. 1,458 card holders</p>	<p>Page 251</p>
<p><b>c) Expand the use of Performance Based Contracting.</b></p>	<p><b>FY 2002</b> Allocate \$207.0 million of the available NIH contracting dollars to Performance Based Contracting (PBC) eligible contracts.</p> <p><b>FY 2001</b> Allocate \$21.2 million of the available NIH contracting dollars to PBC-eligible contracts.</p> <p><b>FY 2000</b> Allocate \$19.8 million of the available NIH contracting dollars to PBC-eligible contracts.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target significantly exceeded. \$198.5 million PBC-eligible contracts.</p>	<p>Page 254</p>
<p><b>d) Identify and pilot new approaches to providing human resource services which increase manager satisfaction with personnel system flexibility and ease of use.</b></p>	<p><b>FY 2001</b> Complete distribution of the final year management satisfaction survey, interviews, and collect and analyze data for the final report due in 2002.</p> <p><b>FY 2000</b> 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.</p>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target not met. Survey indicates a 6% increase in managers' satisfaction.</p>	<p>Page 256</p>



Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 1999</b> Complete the delegations of authority and related training.</p>	<p><b>FY 1999</b> Target met. Delegations completed and related training provided to managers.</p>	
<p><b>e) Implement the Director's overall strategy to improve information technology (IT) management at NIH.</b></p>	<p><b>FY 2000</b> Complete implementation of the technical recommendations.</p> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Ensure Year 2000 (Y2K) compliance for all NIH mission critical systems.</li> <li>2. Complete NIH IT organizational, investment, and vision activities.</li> </ol>	<p><b>FY 2000</b> Target met. Information Technology Central Committee's technical recommendations implemented.</p> <p><b>FY 1999</b> Target met. All 14 mission critical systems Y2K compliant.</p> <p>Target met. NIH IT organization structure revised; new IT investment process established; and IT strategic vision commenced.</p>	<p>Page 259</p>
<p><b>f) Improve compliance with the Prompt Pay Act.</b></p>	<p><b>FY 2000</b> Reduce interest penalties and increase discounts by paying 93 % of invoices on time.</p> <p><b>FY 1999</b> Reduce interest payments and increase discounts by paying 93% of invoices on time.</p>	<p><b>FY 2000</b> Target significantly exceeded. 95% of invoices paid on time.</p> <p><b>FY 1999</b> Target significantly exceeded. 94% of invoices paid on time</p>	<p>Page 262</p>
<p><b>g) Improve customer satisfaction with the quality of products and services.</b></p>	<p><b>FY 2000</b> An 85% overall average rating of approval for procurement offices as measured by the ABS.</p>	<p><b>FY 2000</b> Target met. Average rating of 89% achieved.</p>	<p>Page 264</p>
<p><b>h) Ensure the soundness of the NIH property management system.</b></p>	<p><b>FY 2000</b> Complete the FY 2000 milestones in the personal property improvement plan and achieve a loss rate of no more than 8% of the total property in the inventory.</p> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Complete the activities listed above to resolve the property inventory discrepancies, including the completion of the property inventory, resolution of inventory discrepancies and reviews by the Board of Survey to</li> </ol>	<p><b>FY 2000</b> Target significantly exceeded. Implementation achieved. 4.2% loss rate in FY 2000.</p> <p><b>FY 1999</b> Target substantially met. Physical inventory for 1999 completed. Capital property discrepancies resolved for 1998 survey; significant</p>	<p>Page 266</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>determine the reason for discrepancy and proper disposition of the property.</p> <p>2. Complete the NIH Director and IC Directors review and decision-making and the time lines for implementing the system improvement processes.</p>	<p>fraction of non-capital property discrepancies resolved.</p> <p>Target met. Changes to management practices and procedures announced.</p>	
<p><b>i) Simplify data entry and update into property systems.</b></p>	<p><b>FY 2000</b> Implement the pilot project(s) in one or more of the ICs.</p>	<p><b>FY 2000</b> Target significantly exceeded. Programs based on commercial software implemented in two Institutes. Pilot projects conducted in number of others.</p>	<p>Page 269</p>
<p><b>j) Reduce key time and attendance error rate indices by implementing the Integrated Time and Attendance System (ITAS).</b></p>	<p><b>FY 2000</b> Reduce the benchmark levels of the error rate indices by 20%.</p> <p><b>FY 1999</b> Complete implementation of the ITAS system.</p>	<p><b>FY 2000</b> Target met. Error rates reduced by 20% or more for the four indices monitored.</p> <p><b>FY 1999</b> Target met. Implementation completed.</p>	<p>Page 271</p>
<p><b>k) Ensure that overpayments do not occur in NIH fellowship programs and that bankruptcy statutes are complied with in collecting past over-payments.</b></p>	<p><b>FY 2000</b> Complete implementation of the Fellowship Payment System (FPS).</p> <p><b>FY 1999</b> Complete implementation of corrective measures and begin implementation of the FPS.</p>	<p><b>FY 2000</b> Target substantially met. Institute pilot tests completed and full implementation progressing.</p> <p><b>FY 1999</b> Target met. Implementation of corrective measures completed. FPS implementation progressing as expected.</p>	<p>Page 273</p>

## Performance Goal Details - Priority Setting

**Goal a)      Ensure that NIH-supported research reflects the changing nature of scientific opportunities and public health needs.**

**Performance Targets & Results**

**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 2001-2002 performance to be reported in February 2002 and 2003, respectively.*

**FY 2000**

*Performance: Target met. NIH's Institutes and Centers convened numerous workshops and other meetings that resulted in new programmatic initiatives being issued in FY 2000.*

**FY 1999**

*Performance: Target met. NIH's Institutes and Centers conducted numerous workshops and panels in FY 1999 that assessed scientific progress and opportunities and identified emerging public health needs.*

Note: Given the repeated nature of the activities involved, this goal is marked by an “annual target” which does not change year to year.

### **Goal Background**

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 and include review groups, composed of accomplished investigators established to evaluate grant applications for scientific merit; meetings of national advisory councils, with representatives from the public, medical, and scientific communities, to review a broad range of its policies; external advisory groups to assess NIH-wide activities and to recommend programmatic directions based on changes in the science

and public health needs; and input from representatives of patient and other health advocacy organizations, DHHS, OMB, other federal agencies, and the Congress on a variety of issues of common concern.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

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 Applications (RFAs) that encourage research in areas of identified need.

#### ***Validation and Verification:***

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) and requests for applications (RFA) issued by the Institutes and Centers are publicly available. The content of PAs and RFAs provides a cross-check for consistency with the recommendations from the workshops or other forums.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Sponsorship of Institute and Center workshops and panels that assess the scientific progress and identify emerging public health needs and scientific opportunities. Incorporate the findings and recommendations from these workshops and panels into updated plans, priorities, and proposal submission requests for Institute and Center research programs.**

Target met. NIH's Institutes and Centers convened numerous workshops and other meetings that resulted in new programmatic initiatives being issued in FY 2000.

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.

A list follows below of the FY 2000 Requests for Applications (RFA), Program Announcements (PA), Requests for Contracts (RFC), and other program initiatives that encourage research in

areas of identified need, along with the associated Institute and Center sponsored workshops, panels, and other meetings held to solicit public input on NIH activities.

Assessment Data: RFAs and PAs are published in NIH's *Guide for Grants and Contracts*; RFCs are published in the *Commerce Business Daily*. The agendas and summaries of the workshops and meetings are available and document the specific recommendations forthcoming from the workshops and other forums.

### ***Progress Toward Goal Achievement***

In FY 1999 and 2000, NIH Institutes and Centers identified scientific/public health areas for which workshops and other meetings were held and recommendations made, which led to changes in existing or implementation of new research program initiatives.

Continually reviewing and updating its priorities is essential for NIH to ensure scientific progress, meet national needs, and efficiently use available resources. Convening workshops and other meetings designed to identify public health needs and assess scientific progress ensures that this goal is met annually.

### ***Next Steps***

NIH will continue to convene workshops and panels that identify public health needs and assess scientific progress and opportunities across the spectrum of medical research programs that the agency supports and conducts. NIH will take appropriate actions to implement the recommendations of these meetings.

**Supporting Information for Priority Setting Goal a**

FY 2000 Requests for Applications (RFA), Program Announcements (PA), Requests for Contracts (RFC), and other program initiatives that encourage research in areas of identified need. Cross-listed with associated Institute and Center sponsored workshops, panels, and other meetings held to solicit public input on NIH activities.

The information is organized by GPRA research goal.

<b><i>Research Goal A: Add to the Body of Knowledge about Normal and Abnormal Biological Functions and Behavior</i></b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Electrical Remodeling: Novel Opportunities for Arrhythmia Control B November 1999	Roundtable Conference on Future Research Directions in Atrial Fibrillation B October 1998
RFA, Inflammation in the Pathogenesis of Chronic Obstructive Pulmonary Disease B November 1999	Workshop, AThe Role of Infectious Agents and Atopy in the Development of Chronic Obstructive Pulmonary Disease@ B September 1998
RFA, Oxygen Sensing During Intermittent Hypoxia B November 1999	§Workshop, AMolecular and Genomic Effects of Tissue Oxygen Deprivation in Sleep Apnea@ B September 1998 §Conference, AOxygen Sensing: Molecules to Man@ B June 1999
RFA, Cellular and Molecular Mechanisms of Diabetic Cardiomyopathy B January 2000	Working Group, ACellular and Molecular Mechanisms of Diabetic Cardiomyopathy@ B July 1998
RFA, Ancillary Studies in Heart, Lung, and Blood Disease Trials, June 2000	Conference on Biomarkers and Surrogate Endpoints B April 1999
RFA, Genetic Modifiers of Single Gene Defect Diseases B August 2000	§SPARK Working Group Conference B September 1998 §Workshop, AGenetic Basis of Variability in the Progression and Outcome of Heart, Lung, and Blood Diseases@ B July 1998 §Special Emphasis Panel on Airway Biology and Disease B June 1997
RFA, Genetics Aspects of Tuberculosis in the Lung B September 2000	§Working Group, ATB/AIDS RFA Working Group FY 1999: TB in the Lung Present and Future@ B September 1999 §Special Emphasis Panel, ANew Approaches to Complex Biological Problems: Inflammation and Risk Assessment@ B September 1997
RFA, Research on Alcohol and Sleep B April 2000	Workshop on Alcohol and Sleep B May 1999

<b>Research Goal A: Add to the Body of Knowledge about Normal and Abnormal Biological Functions and Behavior</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Cognitive Approaches to Addictive Processes B July 2000	Cognitive Neuroscience and Drug Addiction: Primed for Interaction B April 2000
RFA, Development of Behavioral Methods for Drug Abuse Studies in Mouse B August 2000	Model Genetic Organisms for the Study of the Nervous System and Behavior B October 1999
PA, Molecular Genetics of Drug Addiction Vulnerability B June 2000	Prospects for the Molecular Genetics of Drug Abuse B October 1999
PA, Developmental Psychopharmacology B June 2000	Intersection of Drug Abuse, Stress and Development B January 2000
RFA, Beta Cell Biology Consortium B October 2000	Stem Cells and Pancreatic Development B April 2000
RFA, Innovative Use of Non-Mammalian Model Organisms to Study Membrane Transport B September 2000	Advances in Membrane Transport: Lessons from Model Organisms B December 1999
RFA, Pathophysiology, Epidemiology and Treatment of Vulvodynia B February 2000	Vulvodynia Workshop: Current Knowledge and Future Directions B April 1997
RFA, Spinal Muscular Atrophy, Amyotrophic Lateral Sclerosis, and Other Motor Neuron Disorders B March 2000	Spinal Muscular Atrophy Workshop B May 1999
RFA, Health Promotion and Disease Prevention: Health Communication, Development and Dissemination B August 2000	Work Group on Single and Multiple Project Grants - May, June, August 1998
PA, Bioengineering Research Partnerships B November 1999	Bioengineering Symposium B February 1998
PA, Skeletal Muscle Perfusion, Aging, and Cardiovascular Disease B February 2000	Changes in Skeletal Muscle Blood Supply With Aging and Disease B May 1998
RFA, Molecular Pathogenesis and New Interventions in Scleroderma B September 2000	Emerging Opportunities in Scleroderma Research B December 1997
PA, Integrative and Collaborative Approaches to Research B May 2000	National Advisory General Medical Sciences Council Subcommittee Meetings B April 1998
RFA, Reannouncement of Large-Scale Collaborative Project Awards B February 2000	National Advisory General Medical Sciences Council Subcommittee Meetings B April 1998
RFA, Pilot Projects for the Protein Structure Initiative (Structural Genomics) B July 2000	Protein Structure Initiative Meeting B April 1998
RFA, Native American Research Centers for Health B August 2000	The Native American Roundtable on Research Training Needs B August 1999

<b>Research Goal A: Add to the Body of Knowledge about Normal and Abnormal Biological Functions and Behavior</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
PA, Centers for AIDS Research and Developmental Centers for AIDS Research B February 2000	Focus Group to Review the Centers for AIDS Research Program B May 1999
PA, Geographic-based Research in Cancer Control and Epidemiology and Small Grants for Geographic-based Research in Cancer Control and Epidemiology B July 2000	Surveillance Implementation Group B March 1999
PA, Self-Management Strategies Across Chronic Illness B June 2000	§Better Health Through Nursing Research: State of The Science Congress B September 1999 §National Nursing Research Roundtable B March 2000
RFA, Innovative Grants on Immune Tolerance B February 2000	Expert Panel on Immune Tolerance B February 1998
RFA, Preparedness Against Illegitimate Use of Bacterial Pathogens B October 2000	Interagency Working Group on Defense Against Possible Bioterrorism B May 1998 and June 1999
PA, Biobehavioral Research for Effective Sleep B January 2000	What is Sleep? What is it Good for? B December 1998
PA, Skeletal Muscle Perfusion, Aging and Cardiovascular Disease B February 2000	Changes in Skeletal Muscle Blood Supply with Aging and Disease B May 1998
PA, Earth-Based Research Relevant to the Space Environment B April 2000	NASA-NIH Joint Workshop Planning Meeting B September 1996
PA, Quality of Life for Individuals at the End-of-Life B August 2000	Symptoms in Terminal Illness B September 1997
PA, Research on Adherence to Interventions for Mental Disorders B December 1999	Research on Adherence to Interventions for Mental Disorders B May 1999
RFA, National Stem Cell Resource B December 1999	Comparative Medicine Workshop on Non Human Embryonic Stem Cells Hosted by the Wisconsin Regional Primate Research Center B May 1998
Complex Chemical Mixtures Interagency Announcement 2000 Science to Achieve Results (STAR) Program	Current Issues on Chemical Mixtures B August 1997



<b>Research Goal B: Develop New or Improved Instruments and Technologies for Use in Research and Medicine</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Microarray-Based Research on Alcohol=s Effects on Behavior, Nervous System Function, and Organ Pathophysiology B April 2000	Workshop on Multiple Hybridization Arrays and Alcohol Research B June 1999
PAS, Bioengineering Research Partnerships B November 1999	Bioengineering Symposium B February 1998
RFP, Biomaterials for the Central Nervous System B March 2000	30th Neural Prosthesis Workshop B October 1999
PA, Technology Development for High-Resolution Electron Microscopy B April 2000	Workshop on High-Resolution Electron Microscopy B July 1999
PA, Advanced Instrumentation for High Resolution Electron Microscopy B April 2000	Workshop on High Resolution Electron Microscopy B July 1999
PA, Cancer Education and Career Development Program B February 2000	§Imaging Sciences Working Group, Meeting of the In Vivo Molecular/ Functional Imaging Subgroup B February 1998 §Cancer Control Review Group B August 1997 §Cancer Prevention Program Review Group B June 1997 §Tobacco Research Implementation Group Report, "Priorities for Tobacco Research Beyond the Year 2000" B November 1998
PA, Development of Novel Imaging Technologies (Phased Innovation Award) and Development of Novel Imaging Technologies: (SBIR/STTR) Initiative B April 2000	§Imaging Sciences Working Group B July 1997 §Lung Imaging Workshop: Technology Transfer B January 1997 §Computer Aided Diagnosis and 3D Image Analysis B October 1998 §Quantitative In-Vivo Functional Imaging in Oncology B January 1999 §Focus Group on Magnetic Resonance §Spectroscopy in Clinical Oncology B April 1999 §BioEngineering Consortium Symposium B June 1999
PA, Mentored Patient-oriented Research for Underrepresented Minorities (K23) B January 2000	§NIH Director's Panel on Clinical Research B December 1997 §Institute of Medicine Committee on Addressing Career Paths for Clinical Research B 1994
PA, Bioengineering Research Partnership B October 1999	BioEngineering Consortium Bioengineering Symposium B February 1998
RFA, Small Business Innovation Research: Animal Models of HCV Infection B November 1999	Biweekly/monthly meetings of the Trans-NIH Hepatitis C Working Group

<b>Research Goal B: Develop New or Improved Instruments and Technologies for Use in Research and Medicine</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
PA, Diabetes Self-Management in Minority Populations B June 2000	Report from Congressionally-Established Diabetes Research Working Group: Conquering Diabetes: A Strategic Plan for the 21 <sup>st</sup> Century B March 2000
PA, Enhancing Adherence to Diabetes Self-Management Behaviors B January 2000	§Diabetes Mellitus: Challenges and Opportunities. Final Report and Recommendations B September 1997 §Congressionally-Established Diabetes Research Working Group: Conquering Diabetes: A Strategic Plan for the 21 <sup>st</sup> Century B March 2000 §Meeting, Behavioral Science Research in Diabetes B November 1999
RFC, Visible Human Project Anatomical Methods, FY 2000	§Seminar on 21st Century Anatomy Applications of the Visible Human Project. §Gross anatomy lecture to first year medical students using the University of California, San Diego=s Anatomic VisualizeR7 software, which was developed using the Visible Human Project image dataset §The Third Visible Human Project Conference B October 2000
RFA, Visible Human Project FdtK Anatomical Methods, FY 2000	Virtual Head and Neck Anatomy Workshop B February 1998

<b>Research Goal C: Develop New or Improved Approaches for Preventing or Delaying the Onset or Progression of Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
PA Centers for AIDS Research B June 2000	Drug Abuse and AIDS: Intertwined Epidemics B July 1999
RFAs, Clinical Centers and Coordinating Center for Prevention and Treatment of Type 2 Diabetes in Children and Adolescents B October 2000	Diabetes Mellitus Interagency Coordinating Committee Meeting: American Indians B May 2000
§PA, Enhancing Adherence to Diabetes Self-Management Behaviors B January 2000 §PA, Self-Management Strategies Across Chronic Diseases B June 2000 §PA, Diabetes Self-Management in Minority Populations B June 2000	Behavioral Science Research in Diabetes B November 1999
RFA, Innovations in Translational Epilepsy Research for Junior Investigators B March 2000	White House Conference on ACuring Epilepsy: Focus on the Future@ B March 2000

<b>Research Goal C: Develop New or Improved Approaches for Preventing or Delaying the Onset or Progression of Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Pediatric Clinical Trials Program for AIDS B September 2000	Workshop, A Detection of Potential Toxicities Following Perinatal Exposure to Antiretrovirals @ B January 1999
RFP, Simian Vaccine Evaluation Units B May 2000	Vaccine Development Resources Group B October 1999
RFA, Cooperative Study Group for Autoimmune Disease Prevention B August 2000	Autoimmune Diseases Coordinating Committee B March 2000
RFP, Malaria Vaccine Production and Support Services B September 1999	§ Component of the Research Plan for Accelerated Malaria Vaccine Development B 1997 § Ongoing external advice provided by the Malaria Vaccine Task Force § Need reiterated at Presidential Millennium Vaccine Initiative B May 2000
RFP, Vaccine and Treatment Evaluation Units: Expanded Phase II & IV Vaccine Trials in Humans B September 2000	Vaccine and Treatment Evaluation Units Review B February 2000
RFA, Long-Term Maintenance of HIV/STD Behavior Change B January 2000	§ Conference on the Role of Families in Preventing and Adapting to HIV/AIDS B July 1999 § Developmental Issues in HIV/STD Prevention with Adolescents B November 1999
RFA, HIV Preventive Interventions for the Severely Mentally Ill B February 2000	Staff meetings with National Alliance for the Mentally Ill representatives B 1999
PA, Ethical, Legal, and Social Implications (ELSI) of Human Genetics and Genomic Research Small Grant Program B September 2000	Ethical, Legal, and Social Implications Research Planning and Evaluation Group Report B September 1997, December 1997; February 1998, April 1998, May 1998, September 1998; March 1999, September 1999
PA, Ethical, Legal, and Social Implications of Human Genetics and Genomic Research Regular Research Grant Program B September 2000	Ethical, Legal, and Social Implications Research Planning and Evaluation Group Report B September 1997, December 1997; February 1998, April 1998, May 1998, September 1998; March 1999, September 1999
PA, Ethical, Legal, and Social Implications of Human Genetics and Genomic Research Education Grant Program B September 2000	Ethical, Legal, and Social Implications Research Planning and Evaluation Group Report B September 1997, December 1997; February 1998, April 1998, May 1998, September 1998; March 1999, September 1999
Research on the Development of Interventions for Youth Violence B January 2000	Workshop on Youth Violence Interventions B October 1999

<b>Research Goal C: Develop New or Improved Approaches for Preventing or Delaying the Onset or Progression of Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, State Models for Oral Cancer Prevention and Early Detection B June 2000	§Workshop on State Models for Oral Cancer Prevention and Early Detection B June 2000 §Workshop on Head and Neck Cancer B February 1999
RFA, The Role of the Environment in Parkinson=s Disease B September 1999	Concept Forum on Parkinson=s Disease B July 1999
RFA, Health Disparities: Linking Biological and Behavioral Mechanisms with Social and Physical Environments B November 1999	Decreasing the Gap: Developing a Research Agenda on Socio-Economic Status, Environmental Exposures, and Health Disparities B January, May, July 1999

<b>Research Goal D: Develop New or Improved Methods for Diagnosing Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Functional MRI and Intervention for Cognitive Deficits after Traumatic Brain Injury B June 2000	Traumatic Brain Injury: Acute Treatment/Long-term Outcome B May 2000
RFA, The Role of Parkin and Related Proteins in Parkinson=s Disease B April 2000	Parkinson=s Disease Planning Meeting reinforced the need and refined the goals of this initiative B January, 2000
PA, Molecular Epidemiology of Prostate Carcinogenesis B March 2000	Prostate Cancer Progress Review Group Report, "Defeating Prostate Cancer: Crucial Directions for Research" B August 1998
Notice, Funding Opportunities Applicable to Breast, Prostate, Ovarian, and Head and Neck Cancers B August 2000	§Breast Cancer Progress Review Group Report, "Charting the Course: Priorities for Breast Cancer Research," B August 1998 §Prostate Cancer Progress Review Group Report, "Defeating Prostate Cancer: Crucial Directions for Research," B August 1998 §Priority Setting Workshop on Head and Neck Cancer B February 1999 §Strategic Planning Conference on New Directions in Ovarian Cancer Research B December 1997 §Colorectal Cancer Progress Review Group B November 2000
RFA, Biological Mechanisms of Noise-Induced Hearing Loss B June 2000	Research Opportunities on the Biology of Noise-Induced Hearing Loss B December 1998
RFA, Ecology of Infectious Diseases B November 1999	Ecology of Infectious Diseases Program Development Workshop B April 1999

<b>Research Goal D: Develop New or Improved Methods for Diagnosing Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Multidisciplinary Clinical Research Centers for Arthritis and Musculoskeletal and Skin Diseases B March 2000	§Meetings that led to publication of Centers Working Group II Report B 1997 §Discussions with Advisory Council and research community B 1998
RFA, Centers for Research to Reduce Oral Health Disparities B September 1999	§Surgeon General=s Conference on Children and Oral Health B June 2000 §Periodic meetings with the Regional centers for Minority Oral Health B 1998-2000

<b>Research Goal E: Develop New or Improved Approaches for Treating Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Studying Spirituality and Alcohol B February 2000	Workshop on Spirituality and Alcohol B February 1999
PA, Collaborations for Advanced Strategies in Complications of HIV Infection B January 2000	Metabolic Disorders in the Pathogenesis of Nervous System Damage in HIV-Infected Drug Users B September 1999
RFA, Study of Viral Resistance to Antiviral Therapy of Chronic Hepatitis C B September 2000	Hepatitis C in African Americans B December 1999
RFA, Gene Therapy Approaches for Diabetes and its Complications B August 2000	Workshop, Gene Therapy Approaches for Diabetes and its Complications B November 1999
RFA, Functional MRI and Interventions for Cognitive Deficits After Traumatic Brain Injury B June 2000	Consensus Conference on Traumatic Brain Injury B October 1998
RFA, Pilot Studies for Re-establishing Connectivity in Spinal Cord Injury B March 2000	Neural Repair and Plasticity Planning Panel Meetings B February 2000
RFA, Pharmacogenetic Research Network and Knowledge Base B April 2000	Understanding Individual Variations in Drug Responses: From Phenotype to Genotype B June 1998
PA, Collaborations for Advanced Strategies in Complications of HIV Infection B January 2000	Working Group, AMetabolic Complications of Antiretroviral Therapies@ B November 1999
RFA, Pediatric Clinical Trials Program for AIDS B September 2000	Working Group, AReview of the NIH Perinatal, Pediatric, and Adolescent HIV Research Priorities@ B June 1999
PA, Diabetes Self-Management in Minority Populations B June 2000	Minority Health Research Development Conference B June 2000

<b>Research Goal E: Develop New or Improved Approaches for Treating Disease and Disability</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
PA, Centers for AIDS Research (CFAR) and Developmental CFAR B February 2000	Program Review B May 1999
RFA, Pediatric Clinical Trials Program for AIDS B August 2000	\$Program Review B June 1999 \$Animal Research Advisory Committee B September 1999
RFP, Specialized In Vitro Immunological Evaluations of Strategies to Combat HIV/AIDS B August 2000	Preclinical Therapeutic Development Committee B 1998-1999
RFA, Asthma and Allergic Diseases Research Centers B March 2000	Extramural Asthma and Allergy Program Review B February 2000
RFA, New Treatment for Complications from Vaccinia Immunization B October 1999	Interagency Working Group on Defense Against Possible Bioterrorism B May 1998 and June 1999
RFA, Anti-Orthopoxvirus Drug Discovery and Development B October 1999	Interagency Working Group on Defense Against Possible Bioterrorism B May 1998 and June 1999
RFA, Challenge Grants: Joint Ventures in Biomedicine and Biotechnology B February 2000	Influenza Challenge Grant Advisory Meeting B November 2000
RFA, International Bioethics Education and Career Development Award B March 2000	First Global Forum on Bioethics in Research B November 1999
RFA, International Studies on Health and Economic Development B May 2000	NIH International Conference on Health and Economic Development B November 1999
RFA, Developing and Testing Innovative Interventions for ADHD B January 2000	Consensus Development Conference on ADHD B July 1998
RFA, Research on the Development of Interventions for Youth Violence B January 2000	NIH Expert Panel on Youth Violence Intervention Research B October 1999
RFA, Host Immune Response to Oropharyngeal Candidiasis	Ad Hoc panel on AIDS Research B April 1997

<b>Research 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.</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
Administrative Supplements for DNA Microarray Analysis B April 2000	Strategic Planning Panels B December 1998
RFA, Orthopoxvirus Genomic and Bioinformatics Resource Center B October 1999	Interagency Working Group on Defense Against Possible Bioterrorism B May 1998 and June 1999
Pathogen Functional Genomics Resource Center B September 2000	Blue Ribbon Panel on Genomics B May 1999
Notice, Administrative Supplements to Support DNA Microarray Facilities B September 2000	Functional Genomics Workshop B September 1999
RFA, Gene Expression Profiling in the Nervous System B November 1999	Genes and Brain Development B April 1999
RFA, Network for Large-scale Sequencing of the Rat Genome B July 2000	Advisory Council Meeting B May 2000
PA, Centers of Excellence in Genomic Science B May 2000	§Five Year planning meetings B May 1997, September 1997, January 1998, May 1998 §Collins <i>et al.</i> , A New Goals for the U.S. Human Genome Project: 1998-2003@ <u>Science</u> 282:682-689, October 1998 §The Biomedical Information Science and Technology Initiative (BISTI) Report

<b>Research Goal G: Work towards the President's goal of developing an AIDS vaccine by 2007.</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, Establishment of Specific Pathogen Free Rhesus Macaque Colonies B February 2000	Ad hoc Advisory Committee on Primate Resource for AIDS Research B June 1999
Innovation Grant Program for AIDS Vaccine Research B January 2000	AIDS Vaccine Research Committee B October 1999
PA, Integrated Preclinical/Clinical AIDS Vaccine Development Program B March 2000	Vaccine Planning Committee Workshops - March 1998 and March 1999
PA, HIV Vaccine Research and Design B May 2000	AIDS Vaccine Research Committee B October 1999

<b>Research Goal G: Work towards the President's goal of developing an AIDS vaccine by 2007.</b>	
<b>Title or RFA/PA/RFP or Brief Description of Follow-up Action in FY 2000</b>	<b>Name of Workshop/Other Meeting Held to Solicit Public Input</b>
RFA, HIV/AIDS Associated Oral Viral Infections B February 2000	Ad Hoc Panel on AIDS Research B April 1997

**Goal b) Progress in responding to the Institute of Medicine Report recommendations for improving public input and priority setting at the NIH.**

<b>Performance Targets &amp; Results</b>
<p><b>FY 2000</b></p> <p>Development of draft strategic plans by each of the research Institutes and Centers.</p> <p><i>Performance: Target met. Each of NIH's Institutes and Centers has developed a strategic plan that addresses its research programs and activities.</i></p> <p><b>FY 1999</b></p> <p>1. Implementation of activities to enhance public input into NIH activities.</p> <p><i>Performance: Target met. NIH established the Offices of Public Liaison (OPL) in the Office of the Director and in each IC; established a Director's Council of Public Representatives (COPR); and took other initiatives related to the role of public representatives on NIH policy and program advisory bodies.</i></p> <p>2. Progress in implementing appropriate recommendations of the Institute of Medicine regarding the NIH priority setting process.</p> <p><i>Performance. Target met. The IOM made a total of 12 recommendations in its July 1998 report, Scientific Opportunities and Public Needs - Improving Priority Setting and Public Input at the National Institutes of Health.@ NIH=s activities in FY 1999 responded to all of these.</i></p>

Note: This goal was completed in FY 2000 and will not be further tracked. Additionally, the FY 1999 targets were erroneously duplicated in the summary table of the previous GPRA FY 1999 Report/FY 2001 Plan as targets for FY 2000 and FY 2001. These targets were met in FY 1999 and were not carried forward.

**Goal Background**

The NIH seeks and receives input from review panels, workshops, and other outside sources regarding NIH activities, including priority setting. Emerging public health problems and the



need to rapidly respond to new research opportunities require that the NIH continually review and implement appropriate recommendations from relevant constituencies. NIH recognizes the value of enhanced public input and has taken specific actions to strengthen its efforts in this regard.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The FY 2000 target reflects the former NIH Director's request that each of the agency's research Institutes and Centers develop, by the end of December 1999, a strategic plan that covers a 2 to 5 year period of time. The Director further requested that the public be involved in the development of these plans.

The information and process for generating these plans will serve multiple purposes, including further informing the Director, NIH and the public about the overall priorities of each Institute and Center; educating the public about the planning process of each Institute and Center; and helping to ensure that the research priorities of Institutes and Centers are responsive to the needs of the public.

#### *Validation and Verification:*

The completed Institute and Center strategic plans will be publicly available, through NIH's Web site and/or print.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Development of draft strategic plans by each of the research Institute and Centers.**

Target met. Each of NIH's Institutes and Centers has developed a strategic plan that addresses its research programs and activities.

Each Institute and Center provided a draft copy of its strategic plan to the Office of the Director at the end of December 1999. A request for clearance for publication of the plans was approved by the Department of Health and Human Services in March 2000.

Assessment Data: The Institute and Center strategic plans are available for review.

#### ***Progress Toward Goal Achievement***

The goal has been achieved.

**Performance Goal Details - Grants Administration and Peer Review**

**Goal a)      Ensure proper stewardship of public funding for research.**

Performance Targets & Results
<p><b>FY 2002</b></p> <p><b>Publish a report of findings, lessons learned, and best practices observed in the conduct and administration of sponsored programs at NIH’s recipient institutions.</b></p> <p style="text-align: center;"><i>Performance to be reported in February 2003.</i></p> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li><b>1. Create an organizational component within NIH with FTE’s devoted expressly to compliance-related activities.</b></li> <li><b>2. Perform a minimum of 10 compliance site visits.</b></li> </ol> <p style="text-align: center;"><i>Performance to be reported in February 2002.</i></p>

Note: This is a new goal in FY 2001.

***Goal Background***

With the receipt of public support, investigators and institutions accept the responsibility to conduct research 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 and the recipient, the need for an effective compliance program is essential. NIH, in an attempt to minimize the risks associated with noncompliance, has taken steps to increase educational outreach, enhance administrative oversight of sponsored research, and, working in partnership with grantees and national professional organizations, renew an institutional commitment to compliance.

An effective strategy to enhance compliance is to develop a proactive grants compliance program that will better enable recipients to understand their stewardship role and for the sponsor to gauge the level of that understanding. Such a proactive compliance program is intended to enhance the ability of recipient and sponsor to assess institutional systems, promote effective stewardship of NIH funds, and develop a culture of compliance that protects the Federal investment.

***Performance Assessment Approach***

*Basis and Data:*

FY 2002: A report of best practices observed in the conduct and administration of sponsored programs at our recipient institutions will mark the achievement of this goal. Progress will be gauged by comparing the audience and content of education and outreach efforts to those in previous years.

FY 2001: Progress will be measured by completion of the paperwork required by the indicated organizational change. Position descriptions of FTE's associated with the new office will be available through personnel.

*Validation and Verification:*

FY 2002: The report will be available on the Web site of NIH's Office of Extramural Research.

FY 2001: The Office of Extramural Research's organizational charts are also accessible through this Web site.

**Goal b) 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.**

**Performance Targets & Results**

**FY 2002**

1. Complete formation of all external IRG Working Groups.
2. Increase number of Steering Committees and Study Section Boundaries Teams from 4 to 10.

*Performance to be reported in February 2003.*

**FY 2001**

1. Increase the number of external IRG Working Groups from 8 to 14.
2. Create 4 Steering Committees and their respective Study Section Boundaries Teams.

*Performance to be reported in February 2002.*

**FY 2000**

1. Enhance study section operations by doubling the number of IRG external advisory groups from 3 to 6.

*Performance: Target significantly exceeded. Ten external working groups were formed – four more than had been targeted.*

2. Complete Phase 1 of Panel on Scientific Boundaries for Review and develop an Implementation Plan for Phase 2.

*Performance: Target met. A Phase 1 final report was completed and a Phase 2 implementation plan developed and initiated.*

**FY 1999**

Conduct various assessments of the functions and organization of NIH study sections.

*Performance: Target met.*

*-- The draft Report of the Boundaries Panel was completed and disseminated to the community for comment.*

*-- The integration of neurosciences and AIDS review in CSR was completed and study sections have been established and are now operative.*

*-- The integration of behavioral and social science review in CSR was completed.*

### ***Goal Background***

Grant applications submitted to the NIH are initially reviewed for scientific and technical merit by peer review groups comprised of extramural research scientists. Within the Center for Scientific Review (CSR), these peer review groups (study sections) are clustered into Integrated Review Groups (IRGs) within a particular area of science. Currently in CSR, there are 121 standing study sections clustered within twenty IRGs.

To enhance oversight of the CSR peer review process, external IRG Working Groups consisting of extramural scientists are forming to monitor and assess whether the study sections within each IRG have the necessary scope and depth of expertise to review applications within their area of science. This is one means of ensuring that the 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. Increasing the number of IRG Working Groups is part of an effort to enhance study section operations.

In addition, a broader look at the entire organization and structure of the CSR peer review system has been undertaken by a Panel on Scientific Boundaries for Review (PSBR) comprised of highly recognized experts in the biomedical and behavioral sciences.

Such measures will ensure that the peer review system will be able to accommodate the review of more and more complex, diverse, and multidisciplinary research proposals. In addition, streamlined review procedures have been developed, whereby only the more meritorious applications are given full discussion at the review group meeting, to accommodate increasing work load.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

The number of external IRG Working Groups in operation is one measure of achievement of this target. Other evidence includes completed modifications to CSR study section organization based on recommendations of the PSBR, Steering Committees, and Study Section Boundaries (SSB) Teams.

#### ***Validation and Verification:***

CSR provides comprehensive data (with periodic updates) on the number of external IRG advisory groups established and in operation. Furthermore, modifications to study section organization are widely disseminated (e.g., via the Web): as proposed, for public comment, and when changes are instituted.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results***

**Target 1: Enhance study section operations by doubling the number of IRG external advisory groups from 3 to 6.**

Target significantly exceeded. The number of IRG functional working groups is now 10 -- 4 more than had been targeted. In addition to three that completed their work in FY 1999, three others have been established and their work completed, another three have been established and their work nearly completed, and one other has been established.

Assessment Data: The number of functional IRG Working Groups is published in CSR's "Peer Review Notes" and, as well, documented in the minutes of the CSR Advisory Committee.

**Target 2: Complete Phase 1 of Panel on Scientific Boundaries for Review and develop an Implementation Plan for Phase 2.**

Target exceeded. The Phase 1 final report has been accepted by the CSR Advisory Committee and is posted on the CSR Web site. An implementation plan for the Phase 2 work of the PSBR has been developed and is also posted on the CSR Web site.

The PSBR recommended clustering study sections into 24 IRGs. Acceptance of the final Phase 1 report has launched CSR into Phase 2, over the course of which study sections will be created to populate the proposed 24 IRGs.

A mock referral for distributing grant applications among the 24 proposed IRGs has been conducted. The next step is to form Steering Committees for each IRG or group of IRGs, depending on the science areas of the IRGs. The Steering Committees will evaluate the mock referral and create SSB Teams consisting of research scientists from relevant scientific committees, a member of the PSBR, CSR staff, and other NIH staff. The purpose of these teams will be to define new study sections and determine the scientific boundaries for each study section within the IRG. In an ongoing example, the Hematology Steering Committee has met, and its members are currently gathering names and recruiting established scientists for the SSB Team.

Assessment Data: The PSBR's Phase 1 final report, which details the conduct of an assessment of overall study section organization, is available to the community on the CSR Web page. The Phase 2 implementation plan is also posted on the CSR Web page. Additionally, an update on the Phase 2 activities of the PSBR has been posted on the CSR Web page which documents establishment of the Hematology Steering Committee.

***Progress Toward Goal Achievement***

The progress toward this goal has been as expected throughout both FY 1999 and 2000.

***Next Steps***

To accomplish this goal, it will be necessary to complete the formation of all external IRG Working Groups. This should be completed in FY 2002. It will also be necessary to complete the formation of Steering Committees and SSB Teams. It is anticipated that four Steering Committees and their respective SSB Teams will be created in FY 2001, and that this will be increased from four to ten Steering Committees and their respective SSB Teams in FY 2002.



**Goal c) Improve Electronic Research Administration (eRA) technology and enhance communication with the extramural community.**

### Performance Targets & Results

#### FY 2002

##### **Integrate the NIH Commons with the Federal Commons.**

*Performance to be reported in February 2003.*

#### FY 2001

1. **Implement electronic progress reporting with all 65 newly on-line institutions participating in the FDP.** (Incomplete FY 2000 target carried forward into FY 2001.)
2. **Begin pilot testing of progress reporting for multi-project mechanisms.** (Incomplete FY 2000 target carried forward into FY 2001.)

*Performance to be reported in February 2002.*

#### FY 2000

1. Full deployment of key ERA business process modules.

*Performance: Target met. Key business process models in the NIH Commons were made widely available for business transactions.*

2. Implement electronic progress reporting with all 65 newly on-line institutions participating in the FDP.

*Performance: Target not met. Only limited progress achieved, due to limited budget resources. Begin pilot testing of progress reporting for multi-project mechanisms.*

3. Begin pilot testing of progress reporting for multi-project mechanisms.

*Performance: Target not met. No new development in FY 2000.*

#### FY 1999

1. Design and test new systems.
2. Streamline post-award reporting, while continuing to ensure appropriate oversight and enhancement of recipient compliance with reporting and accountability requirements.

*Performance: Targets met.*

*-- 1,554 users from 74 organizations within the Federal Demonstration Partnership registered to use the NIH Commons in FY 1999. Logins to the Commons average 36 a day.*

*-- Electronic Streamlined Non-competing Award Process (E-SNAP) began receiving the first electronic applications in a limited pilot in May 1999. As of the end of FY 1999, NIH received 22 e-SNAPs and the pilot had expanded to involve 10 institutions. Updated abstracts collected through the e-SNAP submissions have been made available to the public on-line through CRISP, providing the public with the most up-to-date information on scientific projects funded by NIH.*

**Performance Targets & Results**

-- X-TRAIN is currently in a limited pilot involving fifteen schools. The CNAP, CGAP and Fellowship modules are in the detailed design phase of their development.

-- The Electronic Notice of Grant Award (NGA) system was pilot tested in FY 1998 and fully deployed at the beginning of FY 1999. In the first year of implementation the grantee community has embraced the technology and almost 70% of all notifications of awards are now made electronically. Electronic notifications of grant award (NGA) are generated by IMPAC II, NIH's internal extramural research information management system that works in conjunction with the NIH Commons to accommodate a fully electronic grant life cycle. This service has been made available to all NIH grant and cooperative agreement recipients having the capability to receive NGAs electronically.

-- NIH has also taken a leadership position with the development of the Federal Commons. By assuming this role NIH is assuring that internal progress in the area of ERA will utilize technologies that will be the standards across the government. Standard data dictionaries have been developed in this interagency effort that will allow for easy sharing of information between agencies and departments.

**Goal Background**

Enabling extramural research institutions to use ERA technologies will greatly facilitate preparation of grant applications by research investigators, processing of applications by NIH staff, and management of awards by grantee organizations and NIH staff. NIH has begun development of the NIH ERA Commons, a Web-based client/server environment where the NIH and grantee community will conduct their research administration business electronically. Once the system is fully deployed and operational, the NIH will be able to maintain timely, secure electronic communication with extramural grantee business partners and will have the ability for full electronic research administration from application submission through closeout.

The following modules of the NIH Commons are planned and are in various stages of development/deployment:

- **Status:** The Status interface allows institutional officials and principal investigators, with appropriate security, to access information on the status of pending applications and awards electronically. The module also allows principal investigators to view summary statements with complete confidentiality as soon as the summary statement is completed.
- **E-SNAP and CNAP:** The e-SNAP and CNAP modules allow principal investigators and corresponding administrative officials from grantee organizations to submit and approve all information pertaining to the non-competing continuation in a fully electronic form, without duplication of Form PHS 2590 or submission of any hard copies of the application package. The modules also allow principal investigators to update their

abstracts as the science warrants. E-SNAP accommodates awards eligible for the simplified non-competing award process, whereas CNAP handles the complex awards.

- ❑ X-Train: The X-Train Training Appointment System allows information on trainee appointments that have traditionally been collected on Form 2271 to be submitted electronically. It allows grant administrative officials to record and obtain information about their trainees. X-Train replaces a less efficient Internet-based trainee appointment system that NIH has used since 1996 to collect over 2,000 training appointment forms.
- ❑ Admin: The Admin module supports the establishment, monitoring, and updating of institutional and professional profiles to relieve administrative officials, principal investigators, and key grant personnel from having to re-key information. The system standardizes the information collected on applicant institutions and individuals, thereby minimizing the redundancy of information collected with every grant application.
- ❑ Fellowships: The fellowship module will enable electronic submission of the Public Health Service individual National Research Service Award (NRSA) Form PHS 416-1.
- ❑ CGAP: The CGAP module will accommodate the competing grant award process. Information traditionally submitted on the application for a Public Health Service Grant Form PHS 398 will be submitted through this module.

The Federal Demonstration Partnership (FDP) will be used for piloting new ERA systems. The FDP is a cooperative effort among federal research agencies and 65 research universities and non-profit research centers. The FDP was established to increase research productivity by streamlining the administrative process and reducing the administrative burden on principal investigators, at the same time maintaining responsible and effective stewardship of federal research funds. Thus, these institutions were a natural choice as the first extramural partners to be brought on-line with the NIH's ERA system.

### ***Performance Assessment Approach***

#### *Basis and Data:*

FY 2002 -- Achievement of this target will be measured by the extent of ability to submit information to NIH through the Federal Commons.

FY 2001 -- Achievement of this target will be measured by the number of institutions registered.

#### *Validation and Verification:*

FY 2002 -- The status of NIH's integration with the Federal Commons will be confirmable through publicly available ERA status reports.

FY 2001 -- The number of registered FDP institutions will be confirmable through publicly available ERA status reports.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

#### **Target 1. Full deployment of key ERA business process modules.**

Target met. In FY 2000, the following key business process modules in the NIH Commons were made widely available for business transactions: Registration, Accounts Administration, Status, and Institutional and Professional Profiles. The number of institutions registered to use the Commons increased 234% from 74 to 173, and the number of registered individuals increased 266% from 1,554 to 4,130.

Assessment Data: The number of registered institutions and individuals is tracked and maintained in a database within the NIH Commons. This information is publicly available through NIH eRA status reports.

#### **Target 2. Implement electronic progress reporting with all 65 newly on-line institutions participating in the FDP.**

Target not met. The number of institutions participating in the pilot in FY 2000 increased from 10 to 15. Work is still underway as we adapt to changing technology and address the need for compatibility with other Federal systems.

Assessment Data: Information on the status of the pilots is available from the NIH eRA website (<http://era.nih.gov/>).

#### **Target 3. Begin pilot testing of progress reporting for multi-project mechanisms.**

Target not met. Work is still underway as we adapt to changing technology and address the need for compatibility with other Federal systems.

Assessment Data: Information on the status of the pilots is available from the NIH eRA website (<http://era.nih.gov/>).

***Progress Toward Goal Achievement***

The introduction of new technology and its attendant costs have delayed new electronic research administration systems development in FY 2000. In addition, a restructuring of the management of the eRA effort took place in FY 2000 emphasizing the establishment of user requirements and funding priorities. This restructuring will assist the NIH in allocating its resources between the various enterprise information systems, and ensure that the needs of trans-agency compatibility are addressed.

***Next Steps***

User requirements have been defined and prioritized for the next year of activities (described at <http://era.nih.gov>). Continued enhanced funding will ensure further development and enhancement of eRA systems in FY 2001.

**Goal d) Develop innovative business practices to facilitate government/public interactions.**

<b>Performance Targets &amp; Results</b>
<p><b>FY 2002</b></p> <p><b>Pilot test ways to further simplify SNAP.</b></p> <p><i>Performance to be reported in February 2003.</i></p>
<p><b>FY 2001</b></p> <p><b>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.</b></p> <p><i>Performance to be reported in February 2002.</i></p>
<p><b>FY 2000</b></p> <p>Expedite the processing of the most meritorious grant applications by extending to all NIH Institutes the use of expedited <i>en bloc</i> Council review procedures.</p> <p><i>Performance: Target met. A policy announcement was prepared by the Deputy Director for Extramural Research, and disseminated to all NIH Institutes. This document encourages the adoption of expedited procedures and provides guidance to Institute staff on the proper procedures to follow.</i></p>
<p><b>FY 1999</b></p> <p>Identify approaches to expedite the processing and award of grant applications.</p> <p><i>Performance: Target met. A major impact in expediting the awards process has been the establishment of procedures, including electronic enhancements, to expedite Council concurrence with peer review determination – a procedure called expedited <i>en bloc</i> concurrence. In essence, Council concurrence for certain applications can be obtained prior to the Council meeting, permitting more timely awards.</i></p>

**Goal Background**

NIH has remained committed to evaluating policies and procedures to increase its own efficiency and improve customer service to grantees. The challenge for NIH is to ensure that simplification of grants administration processes and procedures do not diminish the ability to provide appropriate oversight of its research portfolio.

NIH has identified priority areas on which to focus its efforts. One priority involves shortening the time between submitting a research proposal and receiving the research funds. Shortening this cycle means that the highest quality research will begin sooner or that an already productive

research program will continue uninterrupted. Even in instances where funding cannot begin earlier (e.g., funding a competing continuation application must await the end of the previous non-competing segment), earlier *notification* of pending awards provides enhanced stability of the research enterprise.

In addition to streamlining its own processes, NIH works in close partnership with the extramural community and seeks continual feedback on ways to simplify administrative processes for grantees. As an example, in an effort to be responsive to suggestions from the community, NIH intends to begin a small pilot that will allow, at the discretion of each institution, information required in the streamlined non-competing award process (SNAP) to be submitted directly from the PI instead of the business office of the grantee institution.

### ***Performance Assessment Approach***

#### *Basis and Data:*

FY 2002 – Achievement will be measured by the conduct of pilot test of streamlining improvements (e.g., policy changes, electronic upgrades) with the potential to save the time and effort of grantees and NIH staff.

FY 2001 -- Progress on this target will be measured by the number of such applications that receive award or notice of award within 6-7 months of receipt. (For the purpose of this goal, the “most meritorious” applications are generally defined as those with technical merit ratings in the top 15% across NIH.) This information is available in NIH’s IMPAC database.

#### *Validation and Verification:*

FY 2002 – The progress will be a matter of public record, as reported in the status report posted on the OER website.

FY 2001 – IMPAC is a comprehensive database at NIH, built and refined over many years, that covers the agency’s extramural research activities. Included here are records of research contracts, records of in-process grant applications, and inter- and intra-agency agreements. The data in IMPAC is compared to accounting data maintained by NIH’s Office of Financial Management on a daily basis and there is a record of all applications and awards processed by NIH.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

**Target: Expedite the processing of the most meritorious grant applications by extending to all NIH Institutes the use of expedited *en bloc* Council review procedures.**

Target met. Guidance was prepared and disseminated. Policy Announcement 1999-01 encourages the adoption of expedited procedures and provides guidance to Institute staff on the

proper procedures to follow. This document was prepared by the Deputy Director for Extramural Research and disseminated to all NIH Institutes.

Policy Announcement 1999-01 was distributed by e-mail to the Deputy Director for Extramural Research's Institute liaisons. It has also subsequently been incorporated into the Office of Extramural Research's Extramural Policies Web site.

Assessment Data: The policy guidance and its distribution are a part of the agency's public management record.

### ***Progress Toward Goal Achievement***

The dissemination of information and subsequent use of the innovative business practice of expedited Council review procedures is expected to facilitate government/public interaction by making grant funds available more expeditiously and, thereby, enhance the conduct of research. Already, approximately half of the NIH Institutes are either employing the procedures or preparing to do so.

### ***Next Steps***

The Deputy Director for Extramural Research will continue to encourage the implementation across NIH of expedited Council review procedures.

Data from the NIH IMPAC database will be monitored periodically to determine that the most meritorious grant applications are either being awarded in less time than before, or that at a minimum, applicants are being notified sooner of pending award so that their future research planning is facilitated.



**Goal e) Improve grantee reporting of inventions developed with federal funds.**

**Performance Targets & Results**

**FY 2002**

**Integrate Edison into the Federal Commons (a governmental electronic grants and contracts administration system).**

*Performance to be reported in February 2003.*

**FY 2001**

- 1. Identify ways to improve historical invention reporting data.**
- 2. Further educate constituents of their invention reporting obligations.**

*Performance to be reported in February 2002.*

**FY 2000**

Fully establish the Edison electronic invention reporting system for use by all grantee institutions, and expand its use to other government agencies.

*Performance: Target met. The Edison system is capable of being used by all grantee institutions. The number of institutions registered to use Edison in FY 2000 increased by 44% over the previous FY. The number of agencies using Edison increased by 20% in FY 2000.*

**FY 1999**

Enhance recipient compliance with reporting and accountability requirements.

*Performance: Target met. One hundred and eighty nine institutions are now using Edison. This number represents a 40% increase since FY 1998. In FY 1999, an additional two federal agencies have signed Memoranda of Understanding indicating that they will be now use Edison to meet their patent and invention reporting requirements.*

**Goal Background**

The Bayh-Dole Act was enacted in 1980 to ensure the transfer of technology from federally funded extramural research laboratories to the commercial/public sector. The Act stipulates that all grantees must report on inventions, patents, and licenses that have resulted from federally funded research. To support this requirement, the NIH has developed an electronic research

administration system, "Edison," which is designed to receive, store, sort, and provide reports on invention, patent, licensing and invention utilization.

Edison is the first secure interactive Web site developed as part of the NIH electronic research administration system. Use of Edison significantly reduces the 15 cycles of paper correspondence typically involved in patent and invention reporting to 3, dramatically shortening reporting time and effort, as well as making more information available in a usable format for grants administrators.

### ***Performance Assessment Approach***

#### *Basis and Data:*

Demonstrated use of Edison by all grantee institutions registered to do electronic commerce with NIH by the end of FY 2000. Additional federal research agencies will be encouraged to adopt the Edison system for their reporting requirements so that the federal government can implement a common interface for the research community. The number of grantee institutions registered will be monitored through NIH's IMPAC database. In addition, Memoranda of Understanding with participating agencies will verify their use of the system.

#### *Validation and Verification:*

As previous discussed, IMPAC is a comprehensive database at NIH, built and refined over many years, that covers the agency's extramural research activities. Included here are records of research contracts, records of in-process grant applications, and inter- and intra-agency agreements.

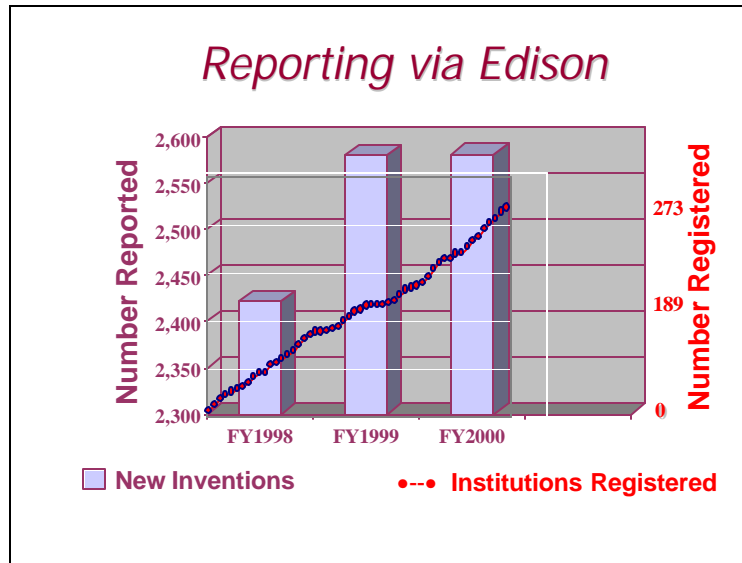
### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Fully establish the Edison electronic invention reporting system for use by all grantee institutions, and expand its use to other government agencies**

Target met. The Edison system is capable of being used by all grantee institutions. In FY 2000, the number of institutions registered to use Edison increased to 273, a 44% increase over the FY 1999 level. The number of agencies using Edison in FY 2000 also increased, from 10 to 12, a 20% increase over the FY 1999 level. Edison is one of the first computer systems to be so widely used across government agencies.



Assessment Data: The reported data were generated through Edison’s computerized tracking system. The database system includes audit capabilities. The number of invention reports received can be derived as needed, and regularly reviewed and reported by NIH management.

***Progress Toward Goal Achievement***

Analysis of trends in NIH award and invention reporting data over time indicate that in excess of 90% of grantee/contractor institutions that do routine invention reporting use Edison to meet their patent and invention reporting needs.

***Next Steps***

In FY 2001, a best practices document will be created, based on proactive compliance site visits that will provide guidance to grantee institutions on their invention and patent reporting systems. Additionally, NIH staff will meet to determine ways to improve the quality of the historical data in the system.

**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.**

Performance Targets & Results
<p><b>FY 2001</b></p> <p><b>Finish meeting the milestones and targets that go beyond the FY 2000 goals.</b></p> <p style="text-align: center;"><i>Performance to be reported in February 2002.</i></p>
<p><b>FY 2000</b></p> <p>Complete the implementation of all recommendations as decided upon by the NIH Director and the IC Directors.</p> <p style="text-align: center;"><i>Performance: Target substantially met. In FY 2000, NIH fully implemented 47 of the Arthur Andersen recommendations. Cumulatively, at the end of FY 2000, 70 of the 76 recommendations (92%) NIH has elected to accept have been implemented.</i></p>
<p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Complete NIH Director and IC Directors review and decision-making for all recommendations.                     <p style="text-align: center;"><i>Performance. Target met. The NIH Director and the IC Directors reviewed the recommendations decided that 76 of the 80 recommendations were appropriate for NIH implementation.</i></p> </li> <li>2. Implement recommendations related to the Chief Information Officer and the Chief Financial Officer.                     <p style="text-align: center;"><i>Performance. Target met. Arthur Andersen recommended that the Chief Financial Officer position be elevated to the Deputy Director of Management level. This recommendation was accepted and implemented. Arthur Anderson recommended that the NIH hire a Chief Information Officer. This recommendation was also accepted and implemented.</i></p> </li> </ol>

Note: Completion of this goal is expected in FY 2001.

**Goal Background**

This initiative is intended to enhance the efficiency and effectiveness of the agency’s business operations. After a seven-month review, Arthur Andersen, Inc. made 80 recommendations regarding administrative costs and practices at NIH. These recommendations included: 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 concluded that 79 of the 80 recommendations were appropriate for NIH implementation. NIH's Arthur Andersen Implementation Oversight Committee subsequently elected not to accept 4 of the recommendations, leaving 76 for implementation.

### ***Performance Assessment Approach***

#### *Basis and Data:*

An Implementation Oversight Committee (IOC) and the Deputy Director of Management (DDM) monitors the review and implementation of the recommendations, with an emphasis on the actions required to deal with priority issues. The IOC and DDM will document recommendation review and implementation. Recommendations identified for implementation will have implementation plans that focus on desired outcomes/outputs to be completed in specific time frames.

A tracking system has been developed to monitor the pace of implementation. Specific quantifiable data will be used, where possible, to provide documentation that the recommendations have been implemented.

#### *Validation and Verification:*

This supporting documentation will validate the completion of recommendations, for example, a redesigned process by a certain date, development of an automated system to replace a manual process, or transition of a certain percentage of an activity from centralized to decentralized.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

#### **Target: Complete the implementation of all recommendations as decided upon by the NIH Directors and IC Directors**

Target substantially met. In FY 2000, 47 of the 76 recommendations that NIH's Arthur Andersen Implementation Oversight Committee elected to accept were fully implemented. Overall, at the close of FY 2000, NIH has fully implemented 70 (92%) of these 76 recommendations.

Assessment Data: This assessment is based on information provided by NIH's Division of Quality Management (DQM) and the Deputy Director for Management (DDM), who monitor the implementation of the Arthur Andersen recommendations. DQM issues quarterly requests for updates from all NIH offices/persons responsible for recommendation implementation.

The Arthur Andersen Management Tracking System, a relational database developed jointly by NIH's DQM and Office of Technology Transfer, has been the quality assurance tool NIH is using to quantify all data related to the implementation of the AA recommendations. An annual report from the AA Management Tracking System was issued to Congress, via the DDM and the NIH Director, for inclusion in the Congressional Record.

### ***Progress Toward Goal Achievement***

Arthur Andersen made 80 recommendations for NIH implementation in its final report issued November 4, 1997. Of the 80 recommendations, the NIH Directors and IC Directors chose not to accept 4 recommendations, leaving 76. At the close of FY 2000, the NIH has fully implemented 70 (92%) of the 76 recommendations that it has elected to accept.

### ***Next Steps***

To date, NIH has fully implemented 70 of the 76 Arthur Andersen recommendations it chose to accept. All recommendations are on schedule to be fully implemented by the end of FY 2001.

To assure that all recommendations are fully implemented on schedule, NIH will:

- Continue current Technology Transfer (TT) leadership activities, and develop a TT Fellowship Program;
- Develop a TT Web-based training tool;
- Implement full e-Commerce capabilities with the NIH New Business System (NBS);
- Implementing a new Cost Accounting System compatible with the NIH Central Accounting System, evaluating system performance on an on-going basis; and
- Clarify NIH IT architecture goals, establishing more standards, and assuring that all new systems are compatible with NIH architecture.

**Goal b) Improve the efficiency of the small acquisition process by continuing to expand the Purchase Card Program.**

**Performance Targets & Results**

**FY 2002**

**\$220 million in orders.**

*Performance to be reported in February 2003.*

**FY 2001**

**\$200 million in orders.**

*Performance to be reported in February 2002.*

**FY 2000**

1. \$160 million in orders.

*Performance: Target met. The volume of orders achieved in FY 2000 was \$173 million.*

2. 3,600 people trained to use cards.

*Performance: Target substantially met. 3,391 people were trained in FY 2000 to use purchase cards.*

3. 2,000 card holders.

*Performance: Target substantially met. At the end of FY 2000, there were 1,729 cardholders.*

**FY 1999**

1. \$110 million in orders.

*Performance: Target met. The volume of orders achieved in FY 1999 was \$130 million.*

2. 3,000 people trained to use cards.

*Performance: Target substantially met. 2,860 people were trained in FY 1999 to use purchase cards.*

3. 1,600 card holders.

*Performance: Target substantially met. At the end of FY 1999, there were 1,485 cardholders.*

Note: The measures used to track this goal are being revised in FY 2001 and beyond, to better focus on the most relevant measure of performance, which is the dollar volume of orders.

### ***Goal Background***

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. Improvements in the reconciliation process are planned to deal with the key complaint of cardholders. The Purchase Card Program is projected to continue to expand, although at a slower rate.

### ***Performance Assessment Approach***

#### *Basis and Data:*

NIH's Office of Administration (OA) will assess performance based on Automated Database reports on purchase card transactions.

#### *Validation and Verification:*

NIH's Automated Data Base (ADB) is a mainframe computer database that integrates acquisition, financial, and inventory information. For acquisition, it is an automated system that tracks orders from requisition through close-out. The bank's purchase card transactions are downloaded into the ADB daily. These transactions represent all NIH purchase card activity for a given day and, when compiled, represent NIH's payment for the 30-day billing cycle. Since information is downloaded directly from the bank, there is full confidence that the number and value of transactions is accurate. In addition, the OA keeps records on the number of card holders and individuals trained as a part of its authorization process.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

##### **Target 1. \$160 million in orders.**

Target met. The volume of orders achieved in FY 2000 was \$173.7 million.

##### **Target 2. 3,600 people trained to use cards.**

Target substantially met. 3,391 people were trained in FY 2000 to use purchase cards.

##### **Target 3. 2,000 card holders.**

Target substantially met. At the end of FY 2000, there were 1,729 cardholders

Assessment Data: The performance figures are based on information from NIH's Automated Data Base (ADB). The ADB is a mainframe computer database at NIH that integrates



acquisition, financial, and inventory information. With regard to acquisition, it is an automated system that tracks orders from requisition through close-out. (For further information see the *Performance Assessment Approach* section above.)

### ***Progress Toward Goal Achievement***

Virtually every study of the government small acquisition process conducted to this point in time has concluded that the use of purchase cards increases the efficiency of the government small acquisition process. NIH has accepted this finding, and the monetary volume of purchases on the purchase cards has increased in each of the last two fiscal years, as has the number of both card holders and people trained to use purchase cards.

In both FY 1999 and 2000, NIH surpassed its target for total dollars spent using purchase cards. It has not, however, met its targets for number of people trained or the total number of cardholders. This outcome is due in part to independent decisions by some Institutes, Centers, and Offices to keep purchase card use somewhat limited. Another factor is that some personnel are opting out of purchase card use, given the associated training and tracking requirements (even though the vast majority of NIH personnel have found not these requirements to be excessive).

These factors will work to constrain growth in the number of card holders and trainees. Nevertheless, as long as total purchases using purchase cards continue to climb in dollar terms, as it has, the broad goal of improving the efficiency of the small acquisition process is being achieved.

In fact, NIH's targets for this goal in future fiscal years will not track the number of either card holders or people trained, as these targets more distracting than helpful in measuring goal achievement.

### ***Next Steps***

As noted above, the projected target of \$160 million for FY 2000 was eclipsed, as final expenditures reached \$173.7 million. And NIH is targeting a purchase card volume of \$200 million in FY 2001, a 20% expansion over the FY 2000 level.

The success of two strategic business decisions is the primary factor behind both last year's increase and the projected future increases. First, the purchase card program expanded outreach efforts by establishing periodic meetings with key personnel from all ICs thereby providing a venue for discussions and problem solving related to the use of the card. Second, specific information technology management program enhancements were implemented in the automated ordering and reconciliation systems. These included a new purchase card log, an automatic reconciliation process, and automatic daily obligations of funds for improved budgetary oversight. NIH anticipates meeting its target by building on the success of these management and technology improvements.

**Goal c)      Expand the use of Performance Based Contracting.**

Performance Targets & Results
<p><b>FY 2002</b></p> <p style="padding-left: 40px;"><b>Allocate \$207.0 million* of the available NIH contracting dollars to PBC-eligible contracts.</b></p> <p style="padding-left: 80px;"><i>Performance to be reported in February 2003.</i></p>
<p><b>FY 2001</b></p> <p style="padding-left: 40px;"><b>Allocate \$21.2 million of the available NIH contracting dollars to PBC-eligible contracts.</b></p> <p style="padding-left: 80px;"><i>Performance to be reported in February 2002.</i></p>
<p><b>FY 2000</b></p> <p style="padding-left: 40px;">Allocate \$19.8 million of the available NIH contracting dollars to PBC-eligible contracts.</p> <p style="padding-left: 80px;"><i><u>Performance:</u> Target significantly exceeded. The dollars allocated to performance-based contracts at NIH totaled \$198.5 million in FY 2000.</i></p>

Notes: This was a new goal in FY 2000.

\*The nearly ten-fold dollar volume increase targeted for FY 2002 primarily reflects a single large performance-based contract in FY 2000.

***Goal Background***

Performance Based Contracting (PBC) allows vendors to be innovative in responding to NIH requirements for specific products and services. In addition, it provides useful indicators of overall contractor performance. As new contract requirements or contract renewals arise, they will be reviewed to determine if use of PBC is appropriate.

***Performance Assessment Approach***

***Basis and Data:***

NIH's Office of Administration (OA) will use the Automated Data Base (ADB) reports and the Information for Management, Planning, Analysis, and Coordination (IMPAC) system to identify contract dollars awarded. The target amounts are based on monies planned for obligation under active performance-based contracts and estimates of amounts expected to be obligated under the newly awarded performance-based contracts.

*Validation and Verification:*

Both the ADB and the IMPAC data bases are used by NIH management for basic management reporting and tracking purposes. Each of the data bases have numerous edits to ensure that the data entered are correct, and Institute OAs are required to reconcile information generated by their systems with their own records to ensure the accuracy of the data on a routine basis.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results***

**Target: Allocate \$19.8 million of the available NIH contracting dollars to PBC-eligible contracts.**

Target significantly exceeded. The dollars allocated to NIH performance-based contracts in FY 2000 totaled \$198.5 million. This amount is ten times the targeted level. One large performance based contract in FY 2000 is the primary reason this occurred.

Assessment Data: NIH's contracting offices -- where the responsibility chiefly resides -- provide the dollar figures for this assessment. These figures reported above are based directly on the records of contracts awarded and funds obligated.

***Progress Toward Goal Achievement***

As indicated, there has been a ten-fold increase in the use of Performance Based Contracting at NIH over the past two fiscal years. This is due primarily to a single, exceptionally large performance-based contract.

Nonetheless, the present expectation is that the dollars and the numbers of performance-based contracts will continue to increase, although at a lesser rate. NIH's increased budget has the potential to increase the number of extramural awards that could be awarded as performance-based contracts.

***Next Steps***

Information presented through small group classroom sessions, meetings and symposia, and consultants are making NIH contracting and program officials more familiar with performance-based contracting. In addition, consultation on individual projects is being provided. And, as contracts are awarded, information on successful performance-based contracts will be disseminated.

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

**Performance Targets & Results**

**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.

*Performance: Target not met. Based on a 1999 managers' survey, there has been a 6% increase in manager satisfaction with personnel system flexibility and ease of use.*

**FY 1999**

Complete the delegations of authority and related training.

*Performance: Target met. Delegations have been completed and related training given to managers who will exercise these authorities.*

*-- NIH has redelegated a number of Title 5 authorities to the ICs as of the end of FY 1999.*

*-- NIH's Office of Human Resources Management (OHRM) conducted briefings for senior managers to inform them of the scope and content of the delegations and of their responsibilities to ensure that they are exercised in a proper manner. More intensive briefings and training were available for managers and administrative staff who will be working with the new authorities on an operating basis.*

*-- OHRM has designed a series of training modules that were available for use by ICs to train managers who will exercise these delegated authorities. Further, several ICs have developed and implemented their own training procedures.*

Note: In an effort to better focus the management/administration-related goals in NIH's annual plans on the most significant issues, the tracking of this goal will be discontinued after FY 2001.

### ***Goal Background***

Following delegation of significant personnel authorities from the DHHS to NIH, the agency has initiated a comprehensive evaluation -- in conjunction with the National Academy of Public Administration (NAPA) -- of the implementation of these authorities.

The NIH Director has redelegated many of the personnel administration and management authorities to Institute Directors to increase the ability of NIH managers to manage human resources more effectively. As of 1997, 10 of NIH's 26 Institutes had redelegated one or more of the twelve human resource authorities available for redelegation.

In 1997, NAPA conducted a baseline survey of NIH managers to assess the utility and flexibility of the agency's personnel systems. The basic findings of this survey were that less than 20% of managers reported the personnel system was 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. A follow-up survey occurred in 1999 and another is planned for 2001.

Additional efforts are underway to identify and pilot new approaches to providing human resource services.

### ***Performance Assessment Approach***

#### *Basis and Data:*

NIH's Office of Human Resource Management (OHRM) will analyze the results of the NAPA surveys of NIH managers. The follow-up survey planned for 2001 will include specific questions to determine managers' satisfaction with the new system. Further, specific criteria and information will be developed for assessing if the new system is in fact providing better results, is easy to use, and if it contributes to the organization's goals and objectives.

#### *Validation/Verification:*

The survey will be conducted independently by the respected National Academy of Public Administration (based in Washington DC).

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: 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.**

Target not met. Based on a 1999 managers survey there has been a 6% increase over the 1997 baseline in manager satisfaction with personnel system flexibility and ease of use. (Although, it should be noted that these data are from the 1999 manager satisfaction survey and do not reflect probable improvements in 2000.)

Of the nineteen categories surveyed, improvement was detected in 18. Improvement of 10% or more was observed in three of the 19 categories. The other 15 categories exhibited improvements of less than 10%.

58% of managers with increased delegations reported a favorable impact on human resource management results that contribute to mission accomplishment. Two thirds of these managers said the delegations have made the personnel system faster and easier to use. However, interviews with a small sample of high level Institute managers and human resource directors suggest that delegations have not gone down deeply enough into the organization and that further redelegation is necessary to achieve their full potential.

A final evaluation is scheduled for the end of FY 2001, which will include another round of the managers' survey.

Assessment Data: The reported data comes from a statistically-valid survey of NIH managers overseen by the National Academy of Public Administration (and conducted by WB&A Market Research).

### ***Progress Toward Goal Achievement***

The goal has been met or exceeded in areas in which delegations have proceeded as expected.

However, interviews with a small sample of high level IC managers and HR directors suggest that delegations have not penetrated far enough and that further redelegation is necessary to achieve the full potential of the system improvements.

The final evaluation is due at the end of FY 2001 and will include another managers' survey.

### ***Next Steps***

NIH will continue to work with Institute managers and human resource directors to promote the redelegation of the authorities to the lowest practicable level. As already observed, it has been shown that these redelegations increase manager satisfaction. Accordingly, further progress towards this goal is anticipated – to be confirmed in the final survey to be conducted in 2001.

**Goal e) Implement the Director’s overall strategy to improve information technology (IT) management at NIH.**

Performance Targets & Results
<p><b>FY 2000</b></p> <p>Complete implementation of the technical recommendations.</p> <p style="padding-left: 40px;"><i>Performance: Target met. The Information Technology Central Committee’s (ITCC) technical recommendations were implemented, in accordance with the established process for managing IT from a NIH-wide perspective.</i></p> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Ensure Year 2000 (Y2K) compliance for all NIH mission critical systems.                             <p style="padding-left: 40px;"><i>Performance. Target met. All 14 of NIH mission critical systems have been determined to be Y2K compliant.</i></p> </li> <li>2. Complete NIH IT organizational, investment, and vision activities.                             <p style="padding-left: 40px;"><i>Performance. Target met. NIH has revised its IT organizational structure under a Chief Information Officer (CIO). The NIH CIO has led the establishment of a new NIH IT investment management process and the development NIH’s IT strategic vision.</i></p> </li> </ol>

Note: Targets for this goal will not be tracked for GPRA purposes after FY 2000. Nevertheless, specific information technology developments at NIH are directly addressed in other sections of the Annual Plan. (See also the *Information Technology Planning* discussion in Appendix 4).

***Goal Background***

In 1996, the NIH Director’s Leadership Forum tasked the Information Technology Central Committee (ITCC) to develop recommendations for centrally managing selected elements of information technology at the NIH. The ITCC addressed the IT organizational structure as well as corporate-wide interoperability between systems and information security practices. Their recommendations have led to the establishment of a process for reaching these over-arching goals even as technology and requirements continue to evolve. The initial steps of the Director’s strategy to hire a Chief Information Officer (CIO) and to establish the Center for Information Technology (CIT) were accomplished in FY 1998. 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 IC IT representatives.

### ***Performance Assessment Approach***

#### *Basis and Data:*

NIH's IT Board of Governors monitors strategy implementation at the agency. This ongoing oversight ensures that major IT projects are on track and achieving the desired goals.

#### *Validation/Verification:*

Documents related to the strategic goals and vision and Investment Review Reports, forwarded to and reviewed by the NIH IT Board of Governors, will confirm the progress on this goal.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

#### **Target: Complete implementation of the technical recommendations.**

Target met. The CIO and his advisory groups have accomplished the following in managing IT from a NIH-wide perspective: 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 an NIH-wide information security program; implemented the technical recommendations set forth by the NIH Information Technology Central Committee (ITCC); and ensured that NIH IT systems and other resources were Year 2000 (Y2K) compliant.

Assessment Data: The minutes of the NIH IT Board of Governors and NIH Information Technology Management Committee (ITMC) document the progress that has been made in managing enterprise IT from a corporate-wide perspective. These minutes can be found at <http://cio.cit.nih.gov/>. This source also provides documentation of the NIH investment review process and the NIH-wide information security program.

#### ***Progress Toward Goal Achievement***

The organizational changes in the management of IT at NIH were designed to facilitate smooth transitions to new technology; a well-managed, secure infrastructure; and integrated systems that support the variety of NIH business processes. The organizational changes also met the requirements of the Clinger-Cohen Act to align IT initiatives with missions and goals, implement a sound and integrated IT architecture, and develop IT investment planning and control processes.

NIH has made much progress in formulating NIH-wide technical standards to facilitate the seamless sharing of electronic information. In establishing CIT, NIH integrated its voice and data communications under one organizational entity. A centralized e-mail system and a network architecture have been established for NIH.



During FY 2000, several pilot projects were implemented to enhance interoperability. One is the development of a NIH Intranet portal that gives NIH extramural, intramural, and administrative communities access to information and NIH applications that are key to the pursuit of their missions via a customized Web interface. In addition, NIH has developed a central, electronic directory pilot project that will contain locator information on each NIH employee and contractor. Initially the information in the directory is associated with the issuance of new employee ID cards coded to indicate an individual's registration for the use of services, such as parking permits and NIH library access. Eventually the electronic directory will share information with a number of other NIH enterprise and IC databases to reduce the redundant entry of information into multiple systems and the number of times that employees must login to separate systems.

The CIO and ITMC continued to collaborate in defining technology directions and guidelines that will enhance and support the electronic exchange of information and the development and support of the enterprise systems, such as the NIH Business System, the Clinical Research Information System, and the Electronic Research Administration System. To facilitate the electronic exchange of information, CIT has implemented the Software Distribution Project that provides site licensed software for commonly used COTS software packages to virtually all of NIH.

In the information systems security area, NIH has developed a proactive, corporate-wide approach. The NIH Incident Response Team (IRT) serves as the focal point for computer security incidents. The IRT identifies computer security incidents, characterizes the nature and severity of incidents, and provides immediate diagnostic and corrective actions when appropriate. The IRT uses the CIT firewall to block specific viruses, incident types, and known hacker IP addresses. In addition, the IRT uses scanning tools, intrusion detection software, and anti-virus software to detect incidents. A communication structure is in place between the IRT and the Institutes and Centers' Information Systems Security Officers where important information is exchanged about incidents.

NIH successfully ushered in the Year 2000 (Y2K), bringing to fruition, a four-year project plan that aggressively addressed the inventory, assessment, remediation, and testing of 404 application systems (including 14 mission critical systems), over 23,000 desktop computers, over 2,000 Unix systems, biomedical equipment belonging to 1490 Principal Investigators (scientists), local area networks, telecommunications networks, and automated building systems in 247 NIH-owned facilities. Contingency planning and effective risk management strategies were pivotal to the smooth transitions through Day One and Leap Year (February 29).

NIH has been successful in establishing a process for managing IT from a NIH-wide perspective. Accordingly, this goal will not be further tracked for GPRA purposes. Further development of NIH's IT systems will of course continue. General information about these activities will be updated in the *Information Technology Planning* section of Appendix 4. In addition, specific information technology developments at the agency will be covered in the other functional areas (e.g., Communication of Results or Grants Administration and Peer Review) of the Annual Plan and Report.

**Goal f) Improve compliance with the Prompt Pay Act.****Performance Targets & Results****FY 2000**

Reduce interest penalties and increase discounts by paying 93 % of invoices on time.

*Performance: Target significantly exceeded. 95% of invoices were paid on time in FY 2000.*

**FY 1999**

Reduce interest payments and increase discounts by paying 93% of invoices on time.

*Performance: Target significantly exceeded. 94% of invoices were paid on time in FY 1999. Interest payments were also reduced. Even though the number of invoices and on-time payment, are trending favorably, the number of discounts taken has actually decreased. The number of discounts taken depends on a number of factors independent of Prompt Payment, and therefore, this measure is not used to gauge the success or failure of this target.*

Note: In an effort to better direct the management/administration-related goals in NIH's Annual Plans at the most significant issues, this goal will not be tracked after FY 2000. (However, information on Prompt Pay Act compliance will continue to be available through other annual NIH accountability documents.)

**Goal Background**

By paying its bills on time, NIH improves relations with the vendor community and saves for research dollars that would otherwise cover late payment interest penalties. In FY 1998, 79% of invoices were paid on time, and in FY 1999 through April, about 92% of invoices were paid on time. Based on technology and process improvements, NIH expected to reduce interest penalties and increase discounts for timely payments in FY 2000.

Because NIH is so decentralized, it is much more difficult for NIH to achieve the 100% level mandated by the Act than it is for most other federal agencies. This goal and its targets are designed to improve NIH as much as possible in this area.

**Performance Assessment Approach****Basis and Data:**

Monitoring data on the timing of invoice payments provided the principal basis for this assessment. NIH's Office of Financial Management (OFM) routinely prepares this information.

*Validation/Verification:*

OFM uses a reporting format that complies with the Prompt Payment Act and has been reviewed and accepted by the Office of the Inspector General (OIG) as a part of the Chief Financial Officer (CFO) audit process. This information can be reported for various time periods and is routinely reconciled to ensure accuracy with accounting records.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

**Target: Reduce interest penalties and increase discounts by paying 93% of invoices on time.**

Target significantly exceeded. 95% of invoices were paid on time in FY 2000.

This achievement helped NIH to improve relations with its vendors.

The amount of interest paid did remain at about \$300,000 per year. However, it is unlikely that this interest can be reduced below this level, when factoring in the approximately \$2 billion of bills paid by NIH each year. These interest payments represent fifteen one thousands of one percent (0.015%) of operations.

The number of discounts depends on various factors independent of Prompt Payment. Accordingly, this particular measure is not used to gauge the success/failure of achievement on this target.

Assessment Data: This performance information is provided by NIH's Office of Financial Management (OFM). (For further details see the *Performance Assessment Approach* section above.)

### ***Progress Toward Goal Achievement***

The present Prompt Pay level of 95% represents a great improvement over the 79% level that prevailed in FY 1998.

The goal has essentially been completed – in fact, significantly exceeded. The extent of compliance is now considered to be at an acceptable level.

This goal will not be further tracked for GPRA purposes. However, Prompt Pay Act compliance information will continue to be available through the agency's annual accountability documents.

**Goal g) Improve customer satisfaction with the quality of products and services.**

### Performance Targets & Results

#### FY 2000

An 85% overall average rating of approval for procurement offices as measured by the Acquisition Balanced Scorecard (ABS).

*Performance: Target met. The average rating of acquisition customer satisfaction measured for the surveyed offices by the ABS was 89%.*

Note: This was a new goal in FY 2000. However, in an effort to better focus management/administration-related goals in NIH's Annual Plans on the most significant issues, this goal will not be tracked after FY 2000.

#### Goal Background

The NIH is participating in the Office of the Secretary's Acquisition Performance Measurement and Improvement Initiatives to develop common intra-agency acquisition performance goals. The system uses a common and balanced set of procurement performance measures developed by DHHS and other federal agencies and is endorsed by the Office of Management and Budget and the President's Management Council.

The Acquisition Balanced Scorecard is a means of assessing customer satisfaction with the acquisition functions provided to 18 Institutes and Centers. The use of the ABS as a model to link performance of critical business processes with organizational goals is widely accepted in government and industry.

#### Performance Assessment Approach

##### *Basis and Data:*

The Office of Administration (OA) used the Acquisition Balanced Scorecard (ABS) to measure performance toward this goal. An ABS survey provides NIH's Office of Contracts Management (OCM) with an overall rating on such factors as quality, timeliness, knowledge, and the overall value of products and services provided. This feedback is useful in identifying key areas for improvement and for planning initiatives to achieve desired customer service goals. When this instrument was used in FY 1998 to survey the customers of three ICs, the average score was 4.1 out of 5.0. Since the original instrument was developed for use within DHHS, the rating scale has been changed from a 5 point scale to a percentage of positive responses. When the ratings

for those offices surveyed in FY 1998 were converted to the new system, 93 percent rated the procurement offices as doing an overall good job. At the end of FY 1999, 6 offices had been surveyed and the results indicated that NIH had an overall average rating of 89 percent. By the end of FY 2000, NIH rated at least 9 of the largest awarding offices.

*Validation/Verification:*

OCM has a contract with the Logistics Management Institute (LMI) to assist in the implementation of the ABS survey. Using the Internet, LMI surveys the individual contracting offices. Reports are provided to each office. OCM reports on the NIH as a whole.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

**Target: An 85% overall average rating of approval from customers of the performance of procurement offices as measured by the Acquisition Balanced Scorecard (ABS).**

Target met. NIH's Office of Acquisition Management and Policy (OAMP) surveyed the customers of twelve acquisition offices responsible for obligating 80% of the contract dollars awarded by NIH. The approval rating for these offices averaged 89%.

OAMP used the Acquisition Balanced Scorecard (ABS), a survey instrument developed by the HHS Office of the Secretary to measure common intra-agency acquisition performance goals. Acquisition customers were asked "Do you agree or disagree that the overall performance of the contracts office is good?"

Assessment Data: The ABS is part of the Office of the Secretary's Acquisition Performance Measurement and Improvement Initiative. The system uses a common and balanced set of procurement performance measures developed by HHS and other participating civilian agencies. The use of the ABS approach has been endorsed by the Office of Management and Budget. (For further details, see the *Performance Assessment Approach* section above.)

### ***Progress Toward Goal Achievement***

This goal has been achieved. It will not be further tracked as a GPRA performance measure.

**Goal h)      Ensure the soundness of the NIH property management system.****Performance Targets & Results****FY 2000**

**Complete the FY 2000 milestones in the personal property improvement plan and achieve a loss rate of no more than 8% of the total property in the inventory.**

*Performance: Target significantly exceeded. Guidance was published to implement the Personal Property Management Improvement Plan. The FY 2000 loss rate was 4.2%, nearly half of the targeted level.*

**FY 1999**

1. Complete activities to resolve the property inventory discrepancies, including the completion of the property inventory, resolution of inventory discrepancies and reviews by the Board of Survey to determine the reason for discrepancy and proper disposition of the property.

*Performance. Target substantially met. NIH completed 100% of the 1999 physical inventory and produced management reports on discrepancies. NIH resolved all capital property inventory discrepancies and resolved a significant part of the non-capital property inventory discrepancies related to the 1998 property inventory. Boards of Survey continue to operate and are expected to remain so.*

2. Complete the NIH Director and IC Directors review and decision-making and the time lines for implementing the system improvement processes.

*Performance. Target met. During the 1998 and 1999 calendar years, Office of Administration (OA) representatives met with IC management personnel, individually and collectively, to announce and to discuss changes to management practices and procedures. The proposed changes included, but were not limited to the delegation of certain property management functions; the conduct of physical inventories; and the institution of Property Survey Boards.*

Note: This goal has been completed. Associated performance measures will not be tracked for GPRA purposes beyond FY 2000.

**Goal Background**

The management of personal property is a major component of the overall management and administrative duties of any organization. This function is easily visible and understandable to the public. Correspondingly, successes and failures are often viewed as an easily available indicator of the administrative health of an organization. At NIH, the critical element in this process is the system of records of accountable property that are maintained by the ICs within the Property Management Information System (PMIS). The accuracy of these records is confirmed by the conduct of physical inventories. The goal of the physical inventory is to assess whether

NIH assets are in the recorded locations and to confirm that all accountable property is appropriately recorded in the management system. All of these measures are ultimately designed to assure that property assets are available for use in support of the various NIH missions and that they are used in an efficient and effective manner.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The Office of Administration (OA) measured progress on the implementation of the personal property management improvement plan. Loss rates were determined from data in the Property Management Information System (PMIS) and from other information such as property loss reports and other discrepancies found in the system that is assembled by the Property Management Division (PMD) inventory support contractor.

The Property Management Improvement Plan includes specific goals and objectives that involve specific outcomes/outputs to ensure the tracking and successful implementation of goals.

#### *Validation/Verification:*

The PMIS database includes several edits and reconciliations to ensure that the data are as correct and accurate as possible. A personal property physical inventory has been completed in each of the past two years to determine if property is being properly recorded and managed. This inventory is used to update the information in the database to ensure accuracy and the proper management of NIH property.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Complete the FY 2000 milestones in the personal property improvement plan and achieve a loss rate of no more than 8% of the total property in the inventory.**

Target significantly exceeded. Implementation of delegations cited in the personal property improvement plan went forward in FY 2000 with institution of the Board of Survey process at NIH's Institutes and Centers. These delegations were incorporated into NIH regulations during the past year. Institute/Center Property Management Representatives and Executive Officers are reviewing additional guidance regarding property management authorities and responsibilities.

With respect to the second part of the target, the FY 2000 loss rate was 4.2% for all accountable items. This considerably surpassed the targeted loss rate of 8%.

Assessment Data: This assessment is based on accomplishments in the publication of revisions to NIH internal regulations and on data obtained in regular reports related to the reconciliation of the FY 2000 inventory of property. (For further details, see the *Performance Assessment Approach* section above.)

***Progress Toward Goal Achievement***

This goal has been completed as envisioned.

In an effort to focus the management-administrative goals in NIH's Annual Plans on the most important issues, the loss rate measure will not be tracked for GPRA purposes beyond FY 2000.



<b>Goal i)      Simplify data entry and update into property systems.</b>
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<b>Performance Targets &amp; Results</b>
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<b>FY 2000</b>
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<b>Implement the pilot project(s) in one or more of the ICs.</b>
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<i>Performance: Target significantly exceeded. Programs based on commercial software were implemented in two Institutes and Centers and pilots conducted in a number of others.</i>
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Note: This was a new goal in FY 2000. However, in an effort to better focus management/administration-related goals in NIH's Annual Plans on the most significant issues, it will not be tracked after FY 2000.

### ***Goal Background***

Many ICs have expressed a desire for a simplified and up-to-date property tracking system. The current Property Management Information System (PMIS) is scheduled to be replaced as part of the new enterprise business system. Until that time, it is felt that a reasonably small expenditure for an off-the-shelf front end for the PMIS will result in significant increases in accuracy and will help to reduce the work effort required to maintain property records.

### ***Performance Assessment Approach***

#### *Basis and Data:*

NIH's Office of Administration (OA) will provide ongoing monitoring/tracking of the implementation of the objectives to simplify data entry into the property system by ICs. Further, specific criteria will be developed to make appropriate decisions for potentially fully implementing a new data entry process. The criteria could include the time required to enter a record, the time to update/reconcile and monitor property, and the accuracy of data.

#### *Validation/Verification:*

Documentation of milestone achievements pertaining to the installation, operation, testing, and appropriate reporting to the ICs of one or more commercial, off-the-shelf, property systems in the NIH environment will provide verification of the progress on this goal.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

#### **Target: Implement the pilot project(s) in one or more of the ICs.**

Target significantly exceeded. During FY 2000, two Institutes and Centers (ICs) implemented programs, using commercially developed software. Pilots were also conducted in other ICs with internally-developed software.

The ICs were provided an opportunity to implement the commercial package NIH-wide. But chose not to do so during the period, due to cost constraints. Nevertheless, implementation of the internally-generated software will provide a satisfactory level of simplification for most activities and should be accomplished with minimal cost implications.

A commercial, off-the-shelf product was implemented in two Institutes. It was decided, however, that, due to the relatively high cost of this product and the impending implementation of the property portions of the Enterprise New Business System (expected within the next three years), NIH would not adopt the commercial product system wide. Although, individual Institutes may still elect to implement this product, if they believe it to be in the interest of their organizations – as two already have.

Assessment Data: The primary basis for this assessment is information from property management staff knowledgeable of Institute & Center progress in implementing these programs. Furthermore, the software procured and currently in place at several ICs provides direct documentation of this progress. During the pilot period, comments, both written and oral, were received from the participating ICs.

### ***Progress Toward Goal Achievement***

Progress on this goal to date has been successful. Pilot project and implementation activities will continue. However, in an effort to better focus management/administration-related goals in NIH's Annual Plans on the most significant issues, these activities will not be tracked beyond FY 2000.

**Goal j) Reduce key time and attendance error rate indices by implementing the Integrated Time and Attendance System (ITAS).**

**Performance Targets & Results**

**FY 2000**  
 Reduce the benchmark levels of the error rate indices by 20%.  
*Performance: Target met. Error rates were reduced by 20% or more for the four indices monitored.*

**FY 1999**  
 Complete implementation of the ITAS system.  
*Performance: Target met. By the end of FY 1999, NIH's Office of the Director (OD) and all 25 ICs had implemented and were running the ITAS timekeeping system. All of these ICs now use ITAS as their sole production timekeeping system. The NIH legacy time-keeping system (TAIMS) is no longer supported.*

Note: This goal was completed in FY 2000 and related performance measures will not be tracked for GPRA purposes in subsequent years.

***Goal Background and Significance***

NIH's Integrated Time and Attendance System (ITAS) project is designed to minimize staff burden and maximize the accuracy associated with recording employee work hours and leave data. This will assure accurate accounting of NIH funds for salaries and benefits.

***Performance Assessment Approach***

*Basis and Data:*

NIH's Office of Human Resources Management (OHRM) will measure and document the improvements achieved for each of several principal error rate indices. After full implementation, OHRM will compare the new data with the benchmarks established in 1998 to determine if the targets are being met. Adjustments to the system/process will be made as needed to ensure the new process is working properly.

When benchmarked in calendar year 1998, the levels of these key indices were: 1,700 payroll error corrections processed; 1,500 missing time and attendance reports; 20,000 time and attendance problem reports; and 1,100 timekeeper initiated corrections as reported by NIH's Automated Data Base (ADB).

*Validation/Verification:*

NIH's Automated Data Base is a mainframe computer database that integrates acquisition, financial, and inventory information.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results***

**Target: Reduce the benchmark levels of the error rate indices by 20%.**

Target met. The 1998 benchmark figures, FY 2000 figures, and % reductions are as follows:

Error Indices	1998	2000	Reduction
PECS Cases	1,700	1,170	31%
Missing T&A Reports	1,500	1,040	31%
T&A Problem Reports	20,000	16,200	19%
TK-Initiated Corrections	1,100	801	27%

Note: The number of PECS cases recorded in FY 2000 was actually 1,560. However, this figure included a proportion of cases that did not involve time and attendance issues or the ITAS system. The adjusted figure represents our best estimate of error correction cases involving time and attendance issues.

Assessment Data: The FY 2000 figures reported above derive from records maintained by the Human Resource Program Support (HRPS) Help Desk. Help desk staff arrived at the figures using biweekly Payroll Error Correction System (PECS) reports, biweekly missing time and attendance (T&A) reports, and Help Desk logs relating to ITAS questions and problems. The timekeeper-initiated corrections figure for FY 2000 was derived based on the number of ITAS active timekeepers, similar to the way that the 1998 figure was calculated.

***Progress Toward Goal Achievement***

The goal has been completed as envisioned. Performance associated with this activity will not be tracked for GPRA purposes beyond FY 2000.

**Goal k) Ensure that overpayments do not occur in NIH fellowship programs and that bankruptcy statutes are complied with in collecting past over-payments.**

### Performance Targets & Results

#### FY 2000

Complete implementation of the Fellowship Payment System.

*Performance: Target substantially met. Full implementation of the pilot test with five Institutes has been completed and full implementation of the Fellowship Payment System is progressing. While still incomplete, overpayment dollars were reduced by 25% due to the new process.*

#### FY 1999

Complete implementation of corrective measures and begin implementation of the Fellowship Payment System.

*Performance: Target met. The implementation of corrective measures is complete. Implementation of the Fellowship Payment System (FPS) is progressing as expected.*

*-- New procedures have been implemented to provide the Office of Financial Management (OFM) with more timely notification of fellows' departures.*

*-- An FPS Working Group has been established to provide oversight of the development and implementation of the FPS.*

*-- Pilot testing of the FPS has begun at five ICs.*

Note: In an effort to better focus the management/administration-related goals in NIH's annual plans on the most significant issues, tracking of this goal has been discontinued after FY 2000.

### Goal Background

Because fellowships involve advanced payments, over-payments sometimes occur in situations involving early terminations or transfers of fellows. To deal with these potential problems, the following measures have been taken: development of a system to certify that a fellow is present and in training, delivery of payments in arrears, timely IC notification to NIH's Office of Financial Management (OFM) about early departures.

A Fellowship Payment System (FPS) Working Group has been established to provide oversight of the development and implementation of the FPS. An action plan has been developed that provides all the milestones needed to implement this system.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The first phase of this goal will be achieved when all ICs are using the new system. The final verification will occur about six months later when the new system will be tested to see if there has been a substantial reduction/elimination of over-payments.

This plan is reviewed on a monthly basis by the Working Group to ensure that the system is implemented on a timely basis. The Working Group measures progress by tracking the pilot test and eventual implementation of the new system. In addition, the NIH's Automated Data Base (ADB) will be used to determine if the amount of over-payments has been reduced.

#### *Validation/Verification:*

OFM operates a system that tracks the amount of overpayments made. Data from this system is reconciled on a monthly basis to ensure the accuracy of the system, and on a yearly basis the system is audited by independent auditors as a requirement of the Chief Financial Officers Act.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

#### **Target: Complete implementation of the Fellowship Payment System**

Target partially met. Full implementation of the pilot test with five ICs has been completed and full implementation of the Fellowship Payment System (FPS) is progressing.

The target was only partially met due to unexpected issues arising during the pilot test. Accordingly, an appropriate management decision was made to revise the implementation schedule.

Significant accomplishments during the fiscal year include:

- Overpayment dollars were reduced by over 25% due to the new process.
- The pilot test phase was successfully completed with 5 ICs.
- NIH-wide Roundtable meeting was held to orient the ICs to the new system.
- FPS II training session has been conducted for all pilot ICs and are continuing for the ICs not yet on the new system.
- New policies and procedures have been drafted for operating under the new environment.

Assessment Data: The Office of Financial Management operates a system that tracks the amount of overpayments made. Data from this system is reconciled on a monthly basis to ensure the accuracy of the system, and on a yearly basis the system is audited by independent auditors as a requirement of the Chief Financial Officers Act.

***Progress Toward Goal Achievement***

The new process has been successful in reducing the dollar level of over-payments by 25% during the past year. As of the end of FY 2000, the ICs using the new system accounted for over 75% of the fellows at NIH. Since the end of the fiscal year, six additional ICs have begun to enter fellows into the system. Also, more than 500 staff NIH-wide have been trained on how to operate the new system.

The current plan is to have all ICs enter fellows into the new system by the end of February. In addition, OFM has placed additional emphasis on the collection of overpayments – resulting in an actual loss of less than \$25,000 during FY 2000. Clearly, for all intensive purposes, this goal has been completed and no longer warrants tracking and oversight.

During FY 2001, the remaining Institutes will be implemented into the new system; FPS III system changes will be completed; and all steps of the work group's implementation plan will be completed. A reduction in the level of overpayments of at least a 50% is expected.

## 2.2 Research Training and Career Development Program

<b>GPRA Research Training and Career Development Program</b>				
<b>FY 2002 President's Budget Request</b> (Dollars in thousands)	<b>FY 1999 Actual</b>	<b>FY 2000 Actual</b>	<b>FY 2001 Estimate</b>	<b>FY 2002 Estimate</b>
	<b>\$811,120</b>	<b>\$912,241</b>	<b>\$1,032,697</b>	<b>\$1,131,739</b>
<b>Major Functional Area</b>	<b>Training Support and Outreach</b> -- Enhance training programs at the predoctoral, postdoctoral, and early career developmental levels to ensure a continuing supply of capable individuals in areas of National need; and encourage participants to pursue research careers and foster the recruitment and retention of under represented groups into careers as researchers.			

### 2.2.1 Program Description, Context, and Summary of Performance

**Program Description and Context.** The Research Training and Career Development Program addresses NIH's longer-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 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 the society's needs for health-related researchers. In addition, NIH's training and career development programs are also designed to enhance the quality and diversity of the biomedical research labor force.

NIH research training and career development support is tailored to the needs of different career levels. For example, students who are beginning graduate training need to learn the conceptual and theoretical aspects of the science they hope to eventually 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. The didactic experiences are normally supplemented with laboratory rotations that help define the frontiers of modern science and the methods used to address current research problems. Lab



rotations also teach students that there are often a number of different experimental approaches to a specific problem. Once students are ready to 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 as research assistant on their mentor's research grant.

This approach to graduate training has been widely praised. NIH research training grants have been such successful vehicles for graduate training that the widely cited report *Reshaping Graduate Education*, published in 1995 by the National Academy of Sciences, recommended that all federal agencies should emulate this approach. A recent NIH evaluation study has also shown 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. These programs clearly encourage institutions to provide high quality training programs and recipients of this support make substantial contributions to the biomedical sciences.

At the postdoctoral level, the NIH supports an extension and expansion of the apprenticeship approach. For individuals remaining in biological or behavioral sciences, the NIH relies on training grants, fellowships, and research assistantships to fund this period of intense research activity focused on the acquisition of the skills and knowledge necessary to launch an independent research career. For clinicians and others with specialized skills and little training in health-related research, the NIH offers career development awards that permit the higher salaries necessary to attract individuals who have completed training in other areas. These awards often include an initial didactic phase to instruct in the concepts the candidate will need as an independent researcher. The candidate then proceeds to an apprenticeship model of training that involves 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.

NIH's Institutes and Centers (ICs) also use the various award mechanisms to recruit individuals from racial and ethnic groups that are currently underrepresented in science. Every NIH research-training grant must have a minority recruitment plan in place prior to award. In addition to this requirement, the NIH also supports the Minority Access to Research Careers and the Career (MARC) and the Career Opportunities in Research (COR) programs of research training grants administered by the National Institute for General Medical Science (NIGMS) and the National Institute for Mental Health (NIMH), respectively. These grants fund research training experiences for honors undergraduates at universities with a substantial minority enrollment, and they serve as an important method of attracting under represented students into careers in health-related research. Minority high school, college, and graduate students as well as postdoctorates and faculty members are supported by Minority Supplements to NIH research grants. Increasing the diversity of the pool of contributing scientists is seen as an important component of reducing the disparity in health outcomes observed in the US population. Finally, the NIH is 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 sciences

women comprise a clear majority of the training pool. However, women are under represented, at the faculty level and within the pool of NIH principal investigators. NIH has initiated a number of programs to address this problem, including career development awards and supplements to research grants to support the re-entry of individuals after a family-related career hiatus.

***Summary of Performance.*** A comprehensive summary table covering all the goals and targets in this program appears at the outset of the functional area discussion on Training Support and Outreach. Please refer to page 284.

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## 2.2.2 Goal-by-Goal Presentation of Performance Goals and Results

### 2.2.2.1 Training Support and Outreach

The overall goal of NIH training and career development programs is maintaining a highly trained population of scientists that can address the nation’s future health-related research needs. To accomplish this important task, the NIH maintains a number of different award mechanisms to provide a flexible and varied series of high-quality training opportunities tailored to the career needs of the recipients. Considerable attention is provided to ensure that the experiences supported address the needs of the trainees and are focused on the acquisition of knowledge and skills necessary to become a productive researcher. Some of these opportunities are listed in the table below:

Name of Award	Activity Code	Description
Institutional National Research Service (NRSA) Research Training Grant	T32	Training grants provide support to institutions which can demonstrate a capacity to assemble a team of high-quality faculty and to attract a suitable number of high-quality students or postdocs interested in engaging in a period of intensive, supervised research training. Training grants are an ideal way to support graduate students prior to the selection of a dissertation subject. It allows the student to consider scientific issues broadly and to rotate through labs as a way to gain exposure to a variety of different approaches to research problems. Training grants also support students and postdoctorates learning the theories and practical aspects of research related to a particular disease or organ system. Other training grants support students in programs leading to a dual research degree such as the MD/PhD.
MARC and COR Research Training Grant	T34	MARC and COR training grants support honors undergraduates at minority serving institutions
Individual NRSA Predoctoral Fellowship	F31	Predoctoral fellowships support supervised training at the graduate level. Special predoctoral fellowships provide support for disabled and minority graduate students.
Individual NRSA Postdoctoral Fellowship	F32	Postdoctoral fellowships support advanced training experiences for doctoral level scientists who need additional research experience in order to successfully compete for independent research funding. Fellows contribute to a defined research project under the supervision of a sponsor or mentor.
Mentored Research Scientist Development Award	K01	The K01 supports mentored career development experiences for fully -trained researchers who may have dropped out of research because of family responsibilities or are switching to a new field of research.
Mentored Clinical Scientist Development Award	K08	The K08 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 that is followed by closely supervised, 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.
Career Transition Award	K22	The K22 is used to support the transition of a postdoctoral researcher to an independent research position. Usually, the postdoctoral researcher applies without institutional affiliation. The K22 offers candidates a provisional award that is activated when a suitable independent research position is negotiated. Some of the K22 awards support and continuing period of postdoctoral experience that is followed by a period of independent research support. Transitional awards operate as a pilot program and NIH Institutes use these awards in different ways. More information is available on the NIH Website at <a href="http://grants.nih.gov/training/careerdevelopmentawards.htm">http://grants.nih.gov/training/careerdevelopmentawards.htm</a>
Mentored Patient-Oriented Research Career Development Award	K23	The K23 is similar to the K08 awards 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.
Midcareer Investigator Award in Patient-Oriented Research Award	K24	The K24 provides up to half-time support for established investigators who want to mentor developing scientists and increase their capacity to conduct high quality patient-oriented researcher.
Clinical Research Curriculum Development Award	K30	The K30 stimulates training in patient-oriented research by offering support to institutions for the development of a curriculum designed to provide the theoretical and conceptual understanding necessary for high-quality clinical research.

The NIH uses these awards and several others (not shown) to carry out the overall goal of maintaining a highly skilled research labor force. This goal is achieved by considering a number of specific priority areas, which include the following:

- **Addressing future needs for researchers.** Planning the approximate number of awards to be made in each category described above is a complex process that considers program continuity and emerging needs. Continuity is important because 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, the NIH tries to maintain a consistent level of support for the overall program. Because students and postdoctoral researchers frequently choose from 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. This is monitored in part by examining application rates for specific programs to ensure they remain attractive career options and serve to recruit individuals into biomedical research. The attractiveness of a particular award can be enhanced by improved outreach, increased benefits for awardees, or increases in the probability of success on

application. For mature programs, that appear to be meeting the needs of the applicant pool, it is important to maintain fairly consistent award rates.

In addition to maintaining existing programs and encouraging institutions to provide training that is sufficiently broad and comprehensive to allow recipients to adapt to changing opportunities, the NIH tries to identify areas that are not being adequately served by current training programs. One such area is patient-oriented research. To address long-standing needs in this area, the NIH established the NIH Director's Panel on Clinical Research to identify specific training needs in the area of patient-oriented research. This panel recommended establishing the *Mentored Patient-Oriented Research Career Development Awards* (K23), *Midcareer Investigator Award in Patient-Oriented Research Awards* (K24), and *Clinical Research Curriculum Development Awards* (K30) awards in FY 1998 to address identified shortages of patient-oriented researchers. The NIH expects to make at least 80 K23 and K24 awards to new and mid-career clinical researchers in each of the next several years. The NIH is also committed to improving the curriculum available to aspiring clinical researchers by funding at least 20 *Clinical Research Curriculum Development Awards* (K30) in FY 1999. Similarly, NIGMS has launched a training program in bioinformatics and computational biology in response to emerging needs.

- ***Estimating future needs for researchers.*** Anticipation of future research needs is very difficult. It is almost impossible to predict major public health needs or shifting research opportunities. Responding to changes is also difficult because of the long time period required for training. Because this is such a difficult area, the NIH engages the National Academy of Science (NAS) every four years, as required by the Public Health Act, Section 489 (P.L. 93-348). In the context of this study, the NIH asks the NAS to analyze trends in the current labor force and attempt to anticipate future needs. The study committee then makes recommendations about the size, quality, and the nature of NIH's training programs. NIH views these studies as very important for identifying special and continuing needs for biomedical, behavioral, and clinical scientists. The eleventh edition of this series of reports called *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists* was released on August 29, 2000 and is available on the NIH website at [http://grants.nih.gov/training/nas\\_report/index.htm](http://grants.nih.gov/training/nas_report/index.htm). NIH will review the recently issued report and develop a plan to implement recommendations with the goal of improving the agency's training and career development programs.

As needs for improvement are identified, the NIH responds in various ways. For example, in 1998, a NIH Director's Panel on Clinical Research identified a specific need in the area of patient-oriented research and recommended establishing the *Mentored Patient-Oriented Research Career Development Awards* (K23), *Midcareer Investigator Award in Patient-Oriented Research Awards* (K24), and *Clinical Research Curriculum Development Awards* (K30) awards to address the identified shortages of patient-oriented researchers. Similarly, NIGMS has launched a training program in bioinformatics and computational biology in response to emerging needs. It is expected that the recommendations in the NAS report, *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists* will generate additional well-identified goals.

- **Maintaining high quality research training programs.** Maintaining the effectiveness of the training and career development programs as well as their impact on the recruitment of bright, young scientists into biomedical research entails a continuing effort. The initial front for maintaining quality, of course, is peer review. The NIH adjusts review criteria and instructs peer reviewers to help identify those applications that are most likely to attract the best trainees and provide the best training. But, in order to assess the overall impact of the programs, the NIH conducts periodic career outcome studies. These studies are coupled with external reviews such as that conducted a quadrennial basis by the NAS (as discussed above). Together, such evaluations help ensure that the NIH research training and career development programs are of high quality and of sufficient magnitude to meet the nation's needs for biomedical and behavioral research. One of the considerations identified in the National Academy's 1993 version of this report (*Meeting the Nation's Needs for Biomedical and Behavioral Scientists*) concerned tracking and evaluation of the careers of training award recipients. In response to this recommendation, NIH launched a comprehensive evaluation of the predoctoral and postdoctoral training programs and is in the process of developing a Web-based tracking system to facilitate future career outcome studies. The specific features of this tracking system are still in the development stage, but will be referred to collectively as *X-Train*. This system will make it easier for training program directors to appoint trainees to training grants, and trainees will find it easier to provide career information to NIH.
- **Addressing issues associated with diversity and health disparities.** NIH remains committed to training and supporting a research community that reflects the nation's racial and ethnic diversity. Accordingly, NIH supports a number of specific training programs like the MARC, COR, Minority Supplements, and the Bridge Program designed to increase diversity within the pool of individuals interested in careers in health-related research. It also maintains several programs that address training needs at the graduate and postdoctoral levels to ensure that individuals from underrepresented groups are retained throughout the period leading to independence. These programs are especially important as the NIH attempts to address disparities in morbidity and mortality across racial and ethnic groups. The involvement of representatives of all segments of the population within the research labor-force will help insure that relevant health and research issues are addressed. In addition to underrepresented racial and ethnic groups, the NIH is also concerned about the involvement of women in research as well as individuals with disabilities. Accordingly, the NIH has specific programs designed to address the retention of these groups in biomedical research careers. An important aspect of these efforts is a continual monitoring of the demographics of the workforce and the population of individuals in training. This ongoing vigilance permits an assessment of the value of existing initiatives and the identification of emerging problem areas.

**Performance Goals Summary Table – Training Support and Outreach**

Performance Goals	FY Targets	Actual Performance	Details
<p><b>a) Maintain adequate application and award rates in key training support areas.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>An application flow consistent with success rates close to the historical levels of 40 percent for fellowships and career awards for basic scientists (F32s and K01s), 60 percent for research training grants (T32s), and 50 percent for entry-level career awards (K08s).</li> <li>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.</li> </ol> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>An application flow consistent with success rates close to the historical levels of 40 percent for fellowships and career awards for basic scientists (F32s and K01s), 60 percent for research training grants (T32s), and 50 percent for entry-level career awards (K08s).</li> <li>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.</li> </ol> <p><b>FY 2000</b></p> <ol style="list-style-type: none"> <li>Maintain an application and award flow consistent with success rates close to the historical levels of 40 percent for fellowships (F32s); 60 percent for research training grants (T32s) and entry-level career awards (K01, K08).</li> </ol>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially met. The FY 2000 success rates were consistent with recent history -- 48% the F32 award; 67% for the T32; 36% for the K01; and 50% for the K08. These awards remain popular with the pool of potential applicants and the quality of applications remains stable.</p>	<p>Page 290</p>



Performance Goals	FY Targets	Actual Performance	Details
	<p>2. Evaluate the effectiveness of the revised announcements, informational materials, and the new training Web site.</p> <p><b>FY 1999</b></p> <p>1. Maintain an application flow that is consistent with success rates close to the historical levels of 40 percent for fellowships (F32s), and 60 percent for research training grants (T32s) and entry-level career awards (K01 and K08).</p> <p>2. Revise and publish announcements related to NIH research training and career development opportunities.</p> <p>3. Reissue the announcement for Minority and Disability Research Supplements.</p> <p>4. Republish the booklet <i>Research Training and Career Development Programs Supported by the National Institutes of Health</i>.</p> <p>5. Re-announce programs as necessary to stimulate the submission of applications.</p>	<p>Target met. Program announcements and policy documents available through NIH's training Web site continue to receive substantial monthly use.</p> <p><b>FY 1999</b></p> <p>Target substantially met. The FY 1999 success rates were consistent with recent history -- 44% the F32 award; 64% for the T32; 37% for the K01; and 52% for the K08. The awards remain popular with the pool of potential applicants and quality of applications stable.</p> <p>Target met. Announcements for the F32, K01, K02, K05, K07, K08, K23, K24, and K30 awards were republished.</p> <p>Target met. The announcements for these awards were published.</p> <p>Target substantially met. A draft of the booklet has been completed and is available on the NIH Web site.</p> <p>Target met. Sufficient progress was achieved, as the standing programs continue to receive a sufficient number of applications.</p>	
<p><b>b) Increase the pool of clinical researchers trained to conduct patient-oriented research.</b></p>	<p><b>FY 2002</b></p> <p>1. Re-announce the career award components of the Director's Initiative on Clinical Research.</p> <p>2. Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p>	<p>Page 299</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 2001</b>                      Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.</p> <p><b>FY 2000</b>                      Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.</p> <p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Re-announce the career award components of the Director’s Initiative on Clinical Research.</li> <li>2. Issue at least 80 awards each in the K23 (Mentored Patient-Oriented Research Career Development) and K24 (Mid-career Investigator Award In Patient-Oriented Research) categories over the course of the fiscal year and at least 20 K30 (curriculum development) awards.</li> </ol>	<p><b>FY 2001</b>                      To be reported in Feb. 2002.</p> <p><b>FY 2000</b>                      Target substantially met. 189 K23 awards were issued; 75 K24 awards.</p> <p><b>FY 1999</b>                      Target met. The K23, K24, and K30 programs were reannounced.</p> <p>Target met 85 K23 awards were issued; 81 K24 awards; and 35 K30 awards.</p>	
<p><b>c) Increase the participation of under represented racial and ethnic groups, women, and individuals with disabilities in NIH training and research programs.</b></p>	<p><b>FY 2002</b>                      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.</p> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Establish new paradigm for measuring the race/ethnicity of NRSA recipients to bring the NIH into compliance with OMB guidelines.</li> <li>2. 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.</li> <li>3. Implement OMB-required race/ethnic data collection and reporting strategy.</li> </ol> <p><b>FY 2000</b>                      Plan action as appropriate to identify and address demographic groups for which interest in training is abnormally low or declining.</p>	<p><b>FY 2002</b>                      To be reported in Feb. 2003.</p> <p><b>FY 2001</b>                      To be reported in Feb. 2002.</p> <p><b>FY 2000</b>                      Target met. NIH enforces minority recruitment requirements on training grants and monitors participation rates.</p>	<p>Page 302</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Prepare a report identifying the demographics of the individuals supported by the NRSA mechanisms and career award mechanisms.</li> <li>2. Issue a Notice of Proposed Rulemaking to permit part-time NRSA support and part-time payback options for individuals with pressing family obligations or disabilities.</li> </ol>	<p><b>FY 1999</b></p> <p>Target not met. Programs have been developed to extract race/ethnicity data on new grant recipients. But the analysis has not yet been completed.</p> <p>Target met. The NPRM was published in the <i>Federal Register</i>.</p>	
<p><b>d) Respond to the National Academy of Sciences quadrennial report on the future needs for health-related researchers.</b></p>	<p><b>FY 2002</b></p> <p>Implement recommendations in the quadrennial assessment of the nation's future needs for biomedical and behavioral research scientists prepared by the National Academy of Sciences (NAS).</p> <p><b>FY 2001</b></p> <p>Prepare an implementation plan related to the NAS report.</p> <p><b>FY 2000</b></p> <p>Respond to the quadrennial assessment of the nation's future need for biomedical and behavioral research scientists issued on August 29, 2000 by the National Academy of Sciences (NAS).</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p> <p><b>FY 2000</b></p> <p>Target substantially met. The National Academy's report has been received. Discussions toward development of an implementation plan are proceeding at the highest level of NIH.</p>	<p>Page 307</p>
<p><b>e) Expand capabilities for electronic administration of research training and career development activities.</b></p>	<p><b>FY 2002</b></p> <ol style="list-style-type: none"> <li>1. Nearly all training appointments are received electronically.</li> <li>2. At least 50% of all termination notices are received electronically.</li> <li>3. Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies.</li> </ol> <p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. At least 50% of all training appointments received electronically.</li> </ol>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p>	<p>Page 310</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p>2. All electronically received appointment information is used to establish trainee appointment records and personal profiles within the IMPAC II system.</p> <p><b>FY 2000</b></p> <p>1. Increase by 40% over the 1999 number of trainee appointment forms received electronically.</p> <p>2. 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.</p> <p>3. Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies.</p>	<p><b>FY 2000</b></p> <p>Target not met. Work is still underway.</p> <p>Target not met. Progress on X-Train and external access to the NIH Person Database has been delayed.</p> <p>Target not met. As data is not yet being collected via X-Train , it is premature to engage in the development of long-term evaluation plans.</p>	
<p><b>f) Improve the capabilities for career outcome tracking for NIH training and career development programs.</b></p>	<p><b>FY 2002</b></p> <p>Develop the second version of X-Train as a source of information on trainees. Use information from X-Train to establish a professional profile for all trainees. Use the professional profile as a source of long-term career tracking information.</p> <p><b>FY 2001</b></p> <p>1. Complete a report on the career outcomes of recipients of NIH extramural postdoctoral research training support.</p> <p>2. Conduct early evaluation of the K23 program based on focus groups composed of recipients.</p> <p><b>FY 2000</b></p> <p>1. Initiate preliminary work on the long-term tracking database.</p> <p>2. Complete a report on the career outcomes of recipients of NIH extramural predoctoral research training support.</p>	<p><b>FY 2002</b></p> <p>To be reported in Feb. 2003.</p> <p><b>FY 2001</b></p> <p>To be reported in Feb. 2002.</p> <p><b>FY 2000</b></p> <p>Target not met. The NIH Person Database has not yet been established as a source for long-term tracking information.</p> <p>Target met. A report on the early careers of NRSA predoctoral trainees and fellows has been completed.</p>	<p>Page 314</p>

Performance Goals	FY Targets	Actual Performance	Details
	<p><b>FY 1999</b></p> <ol style="list-style-type: none"> <li>1. Complete an evaluation study of NIH pre- and post-doctoral training programs based on existing data.</li> <li>2. Add training activities functions to the NIH Commons.</li> </ol>	<p><b>FY 1999</b></p> <p>Target not met. A draft report of the predoctoral study has been completed. Analysis of the post-doctoral data is as yet incomplete.</p> <p>2. Target not met. Due to interface problems with the NIH Commons, the X-Train software is not yet operational.</p>	

**Performance Goal Details - Training Support and Outreach**

**Goal a) Maintain adequate application and award rates in key training support areas.**

**Performance Targets & Results****FY 2002**

- 1. An application flow consistent with success rates close to the historical levels of 40 percent for fellowships and career awards for basic scientists (F32s and K01s), 60 percent for research training grants (T32s), and 50 percent for entry-level career awards (K08s).**
- 2. 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.**

*Performance to be reported in February 2003*

**FY 2001**

- 1. An application flow consistent with success rates close to the historical levels of 40 percent for fellowships and career awards for basic scientists (F32s and K01s), 60 percent for research training grants (T32s), and 50 percent for entry-level career awards (K08s).**
- 2. 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.**

*Performance to be reported in February 2002*

**FY 2000**

- 1. An application and award flow consistent with success rates close to the historical levels of 40 percent for fellowships (F32s); 60 percent for research training grants (T32s) and entry level career awards (K01, K08).\***

*Performance: Target substantially met. In FY 2000, the success rate for F32 applications was 48%; 67% for the T32 category; 36% for K01; and 50% for K08. These success rates are consistent with recent history. These NIH awards remain popular with the pool of potential applicants, and the quality of applications remains stable.*

- 2. Evaluate the effectiveness of the revised announcements, informational materials, and the new training Website.**

*Performance: Target met. Updated announcements for research training and career development programs were incorporated into the NIH Training Web site. The program announcements and policy documents available through this venue continue to receive substantial monthly use.*

## Performance Targets & Results

### FY 1999

1. Maintain an application flow that is consistent with success rates close to the historical levels of 40 percent for fellowships (F32s), and 60 percent for research training grants (T32s) and entry-level career awards (K01 and K08).\*

*Performance: Target substantially met. A sufficient number of applications were received in FY 1999 to maintain a consistent NIH contribution to the support of training in health-related science. Also, success rates were sufficiently close to historical rates for Individual Fellowships (F32s), Institutional Research Training grants (T32s), Mentored Research Scientist Development Awards (K01), and Mentored Clinical Scientist Development Awards (K08) to indicate that the number of applications was relatively consistent and that high quality applications were available for funding.*

2. Revise and reissue announcements related to NIH research training and career development opportunities.

*Performance: Target met. Announcements for the F32, K01, K02, K05, K07, K08, K23, K24, and K30 were republished. The F32 and K12 have been drafted and discussed within the NIH and will be published in January 2000.*

3. Reissue the announcement for Minority and Disability Research Supplements.

*Performance: Target met. Announcements for the Minority and Disability Supplements were published in May, 1999.*

4. Republish the booklet *Research Training and Career Development Programs Supported by the National Institutes of Health*.

*Performance: Target substantially met. A draft of the booklet has been completed and is available on the NIH Website.*

5. Re-announce programs as necessary to stimulate the submission of applications.

*Performance: Target met. The standing programs have received a sufficient number of applications so that programs need not be re-announced for this purpose. Application rates for the most common research training and career development programs remain close to historical levels.*

Notes: The FY 1999, 2000, and 2001 targets dealing with program announcements and other outreach activities were part of a separate outreach goal in the FY 2001 and earlier Annual Plans.

\*The previously published FY 1999 and 2000 statements for Target #1 erroneously associated the K01 award with a historical success rate of 60%. The appropriate target for this award is 40%. (See the *Discussion of FY 2000 Results* section for further details.)

### **Goal Background**

Application rates and award rates for NIH training and career development programs are rough but important indicators of the continuing attractiveness of these programs to the research

community. Application rates provide qualitative information about the utility of individual award options. For example, if the application rate were to fall precipitously for a particular award, the NIH might attempt to determine if eligibility requirements exclude substantial segments of the applicant population or if particular provisions of that award remain competitive with other opportunities. Sometimes potential applicants just need to be reminded that a program is still in operation. In that case, just re-announcing may be sufficient to encourage applications. The NIH typically examines all these options.

To provide an example of how these types of considerations are used, a recent analysis indicated a shortage of clinicians in biomedical research and in particular a shortage of researchers with the skills necessary for research involving human subjects. To address this shortage, the NIH developed the previously mentioned *Mentored Patient-Oriented Career Development Award* (K23). The features of that award were patterned after the *Mentored Clinical Scientist Development Awards* (K08) which had been available to support similar career development experiences for many years. But, because salaries and research expenses provided by the K08 had not been changed for several years and because the environment within the academic medical center has been squeezed economically, institutions were no longer in a position to provide as much additional support for research training and career development experiences. Accordingly, in creating the K23, the NIH issued new announcements with enhanced salary and benefits as a way to encourage the training of more patient-oriented researchers. Over the next several years, the NIH will closely monitor application and award rates to make sure this national need is being addressed.

The success rate of applicants in obtaining funding is also an important factor in ensuring an award is attractive to potential applicants. If an applicant perceives that his/her chances of getting an award are small, he/she will opt for other sources of support. At the same time, success rates are a rough indicator of the quality of award recipients. For specific awards like the *Individual NRSA Postdoctoral Fellowships* (F32), success rates have traditionally been between 35 and 45 percent. This means the selection of these applications for funding is a fairly stringent process. By maintaining a success rate in this range, applicants have a realistic sense of their likelihood of award. For awards like *Institutional National Research Service (NRSA) Research Training Grants* (T32), there is considerable self-selection because the application includes extensive information about the success of former students and postdoctorates. Because of this self-selection and the fact that applicants are normally well established faculty who understand the NIH review system, a considerably higher success rate (near 60%) is more typical and desirable. Even so, it remains important to maintain some stability in the overall success rate so that applicants know what to expect.

Application rates are also affected by the availability of information on award options and the level of technical support provided to the community by NIH staff. Normally programs are announced every three years so that potential applicants are aware that particular programs are still available. The process of re-announcing these programs also offers an opportunity for NIH staff to collectively consider whether the provisions of the award or the eligibility criteria need to be adjusted. NIH staff also engage in various outreach efforts to let prospective applicants know about careers in research and the availability of financial support. These functions are carried out in a number of ways:



- ❑ NIH 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. NIH staff distribute printed information at these conferences and provide individualized advice about appropriate programs and the means to access newly published information.
- ❑ NIH issues announcements in the *NIH Guide to Grants and Contracts*. This NIH resource is available at <http://grants.nih.gov/grants/guide/index.html> and serves as a vehicle for announcing all NIH grant programs. This document is sent each week to an extensive listserv as a means of ensuring that all interested applicants have the information they need to apply for NIH programs.
- ❑ NIH has also developed an extensive website that provides information on research, research training, and career development opportunities in both the intramural and extramural programs, as well as links to job listings and various types of career resources for scientists (<http://grants.nih.gov/training/>). This website organizes the information published in the *NIH Guide for Grants and Contracts* into a logical and easy to access format.
- ❑ Additionally, a popular booklet published by NIH, *Research Training and Career Development Programs Supported by the National Institutes of Health*, is available on the NIH website (<http://grants.nih.gov/training/extramural.htm>). The material is organized by career level and contains tables of different programs designed to help students and postdocs locate appropriate NIH-funded opportunities. These tables include NIH-funded programs that are available at universities as well as programs that require a separate application to the NIH.
- ❑ The NIH homepage receives more than 7 million hits per month and is one of the most frequently consulted websites offered by the Federal government. The research-training page is the 6<sup>th</sup> most frequently hit page on this site – and constitutes an important and growing part of NIH's outreach effort.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

Performance will be gauged by the number of applications and awards for NRSA training grants (T32), individual NRSA postdoctoral fellowships (F32), and individual career development award applications (K01, K08). Data from NIH's Information for Management, Planning, Analysis and Coordination database (IMPAC) will be used to enumerate the total number of applications received and the total number of applications awarded during this time period. Additionally, the number of downloads from the NIH Website continues to be monitored. NIH also meets with potential users of its Web site to discuss the usefulness of the displays.

*Validation and Verification:*

IMPAC is a comprehensive management database at NIH, that has been built and refined over many years and covers the agency's extramural research activities. Included are records of research contracts, records of in-process grant applications, and inter- and intra-agency agreements. The data in IMPAC is compared to accounting data maintained by NIH's Office of Financial Management on a daily basis, and there is a record of all applications and awards processed by the NIH.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results***

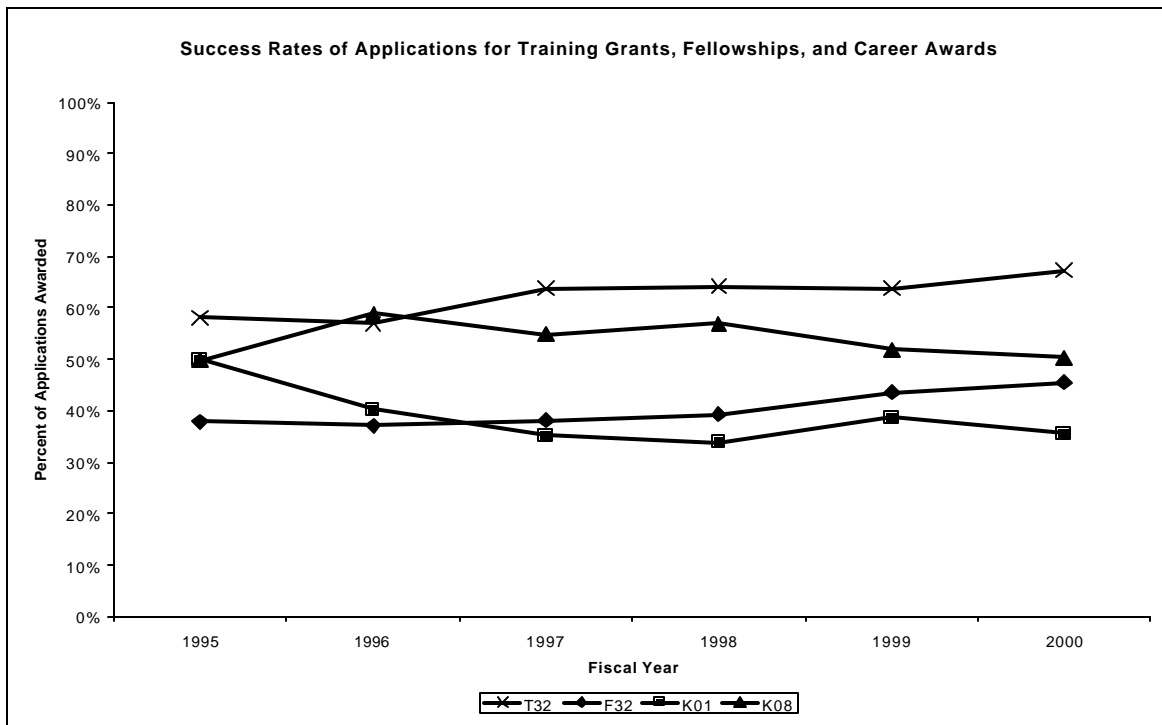
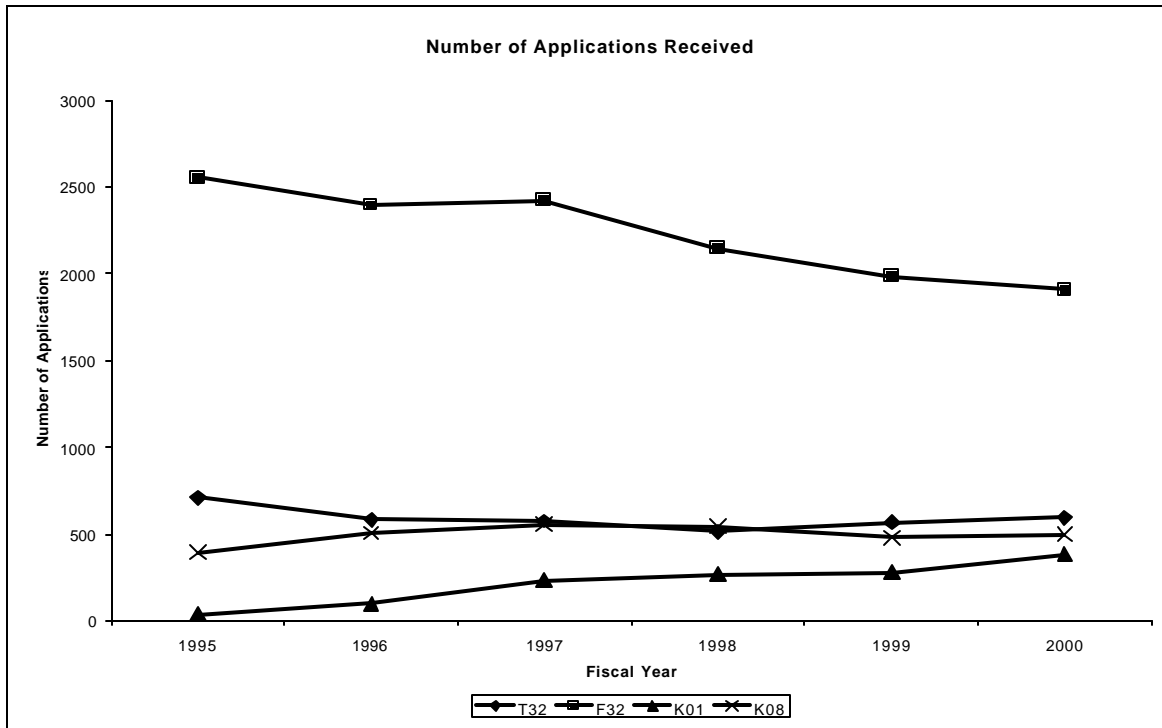
**Target 1: An application and award flow consistent with success rates close to the historical levels of 40 percent for fellowships (F32s); 60 percent for research training grants (T32s) and entry level career awards (K01,K08).\***

*\*Note:* Both the FY 1999 and 2000 published statements of this target *incorrectly* associated the K01 award with a historical success rate of 60%. As the 1995-2000 data in the success rate chart below indicates, 40% is, instead, the appropriate success rate target for the K01 awards.

Target substantially met. In FY 2000, 46% of the 1,906 applications received for postdoctoral fellowships (F32) applications were awarded. 67% of the 594 applications received for research training grants (T32) were awarded. 36% of the 380 applications for Mentored Research Career Development Awards (K01). And 50% of the 495 applications for Mentored Clinical Scientist Development Awards (K08).

These success rates are consistent with those of recent history. This suggests that these NIH awards remain popular within the pool of potential applicants and, further, that the quality of the applications remains stable.

The charts immediately below provide figures on both the numbers of applications received and the fraction of awards for these categories of training and development awards for FY 1995 through 2000.



There has been a slow decline in the number of F32 applications since FY 1995 -- which is cause for some concern. However, this change may be due, in part, to an increased number of K01 awards, as well as the emergence of the Career Transition Award (K22). These awards all

compete for the same applicant pool. Nonetheless, in spite of these changes, the fraction of F32 applications receiving awards has remained relatively close to historical rates.

Similarly, approximately 40 percent of K01 applications have received awards. These award rates for F32 and K01 applications are consistent with the expectation that most applicants possess considerable prior research experience. Accordingly, these applications are held to rather stringent standards. The change in success rates for K01s after FY 1995 may relate to the NIH decision to consolidate various career awards that had previously been used by NIH and the Alcohol Drug Abuse and Mental Health Administration (ADAMHA). The consolidation of differing career awards was a response to the merger of the two agencies in 1993.

The number of research training grant applications (T32) have been very constant since FY 1995 and the success of those applications in review has remained around 60 percent.

The number of K08 applications received has also remained relatively constant at approximately 500 per year. With the advent of the Mentored Patient-Oriented Research Career Development Award (K23) in FY 1999, some reduction in the number of K08 applications can be expected in future years. Because K08 applicants will have more of a molecular (rather than clinical) focus in future years, a decrease in success rates could also emerge.

Assessment Data: The information reported comes from NIH's IMPAC database. (See the *Performance Assessment Approach* section above for further details.)

**Target 2: Evaluate the effectiveness of the revised announcements, informational materials, and the new training Web site.**

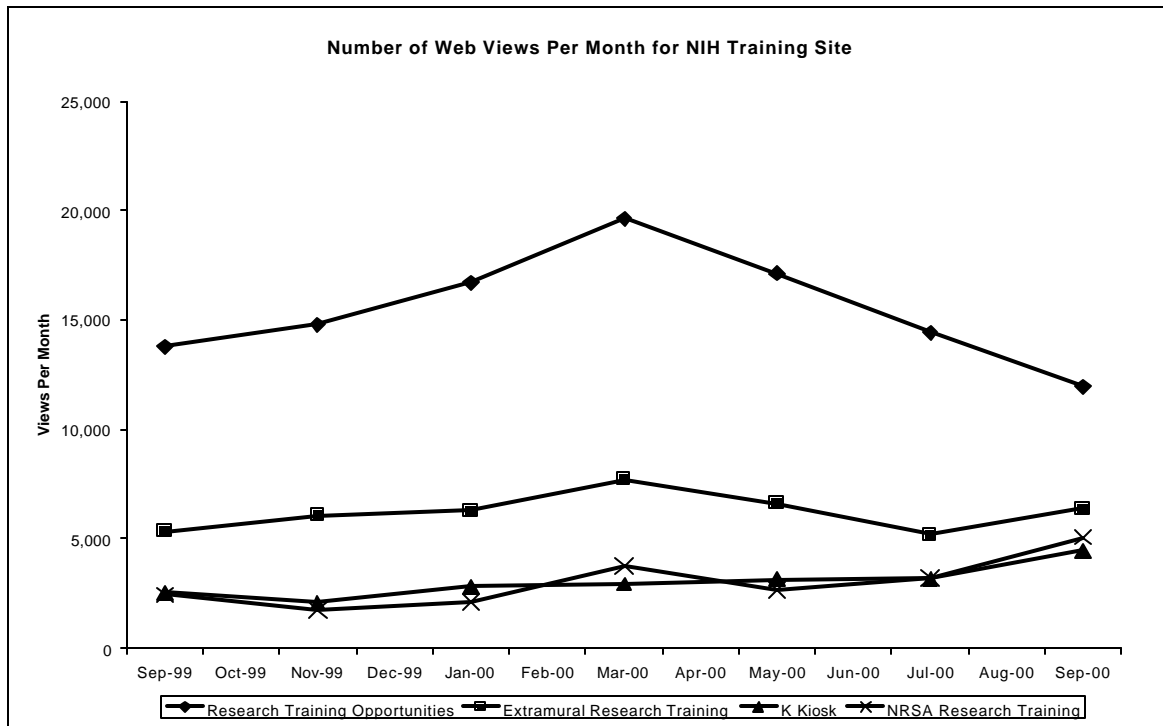
Target met. During FY 2000, most of the program announcements for NIH research training and career development programs were updated. Also, all of the announcements have been incorporated into both the NRSA Web page (<http://grants.nih.gov/training/nrsa.htm>) and into the K Kiosk (<http://grants.nih.gov/training/careerdevelopmentawards.htm>). Additionally, a "K-Wizard" has been added to the Kiosk, which helps potential applicants identify the most appropriate program considering their career goals.

The NIH Training Web site serves as a primary vehicle for dissemination of new program announcements and other policy information related to NIH training and career development programs. The program announcements and policy documents available through this venue continue to receive a substantial number of "hits" monthly from Web users -- an indication of effectiveness and utility.

Web utilization statistics have been collected as shown in the chart below. Since March 2000, the number of views of the transitional Web page "Research Training Opportunities" (<http://grants.nih.gov/training/>), which serves to route users to information on both the Intramural and the Extramural training programs, have decreased while the number of views of the redesigned and updated pages related to NRSA awards and Career Development Awards have increased. The more general page of information on Extramural Research Training Mechanisms

(<http://grants.nih.gov/training/extramural.htm>) has received a fairly constant number of visits during the period examined.

The most important observation is that Web pages containing program announcements and other policy details of the NIH training and career programs are becoming more popular to the user community.



Assessment Data: The information has been generated through WebTrends site analysis software. This measures the number of times a particular page is accessed, how much time the user spent on that page, information about the type of browser used, and the Internet Protocol address of the user's server. This type of data is widely used to assess the value of Web pages. Other similar analyses show that NIH's Web site is one of the most popular federal Internet destinations. The NIH Training pages continue to receive a substantial number of the total views. Further information is available at [http://odoerdb2.od.nih.gov/webstats/2000\\_10/REPORT.HTM](http://odoerdb2.od.nih.gov/webstats/2000_10/REPORT.HTM).

**Progress Toward Goal Achievement**

NIH research training grants, fellowships and career development programs appear to remain an attractive option for training support at different career levels. Application rates remain high and the number of individuals seeking information on these programs that use the NIH Web site appears to be increasing. We believe it is important to monitor both indicators to identify possible changes in the level of interest in these national programs.

***Next Steps***

NIH will continue to monitor the application and award rates for its career development and research training programs. It will also continue to monitor the rate of dissemination of policy and award information via the Internet. Issues pertaining to the successful management of these programs will be addressed as they arise. For example, the concerns about the declining number of F32 applications will be addressed by reissuing the program announcement. Additionally, NIH will seek to increase the attractiveness of this award by raising both the stipend and the funds available under the institutional allowance that provides a partial offset for health insurance in FY 2001.

**Goal b) Increase the pool of clinician researchers trained to conduct patient-oriented research.**

### Performance Targets & Results

#### FY 2002

1. Re-announce the career award components of the Director's Initiative on Clinical Research.
2. Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.

*Performance to be reported in February 2003.*

#### FY 2001

Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.

*Performance to be reported in February 2002.*

#### FY 2000

Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.

*Performance: Target substantially met. NIH made 189 K23 awards and 75 K24 awards in FY 2000.*

#### FY 1999

1. Re-announce the career award components of the Director's Initiative on Clinical Research.

*Performance: Target met. The K23, K24, and K30 programs, which are part of the Director's Initiative on Clinical Research, were reannounced in October and November of this year.*

2. Issue at least 80 awards each in the K23 (Mentored Patient-Oriented Research Career Development) and K24 (Mid-career Investigator Award In Patient-Oriented Research) categories over the course of the fiscal year and at least 20 K30 (curriculum development) awards.

*Performance: Target met. NIH made 85 K23 awards, 81 K24 awards, and 35 K30 awards.*

### Goal Background

Recommendations for increasing research capacity in the area of patient-oriented research stemmed from an NIH Director's Panel on Clinical Research and an Institute of Medicine (IOM) Committee on Addressing Career Paths for Clinical Research. Both groups identified a need to

increase the pool of clinical researchers who can conduct patient-oriented studies, in order to capitalize on the discoveries based on molecular approaches and translate them to clinical settings. The recommendations included expanding and improving training programs in patient-oriented research for both entry-level and mid-career clinical investigators.

Accordingly, NIH established three new career development mechanisms: (1) the *Mentored Patient-Oriented Research Career Development Awards* (K23) for the support of young investigators; (2) the *Midcareer Investigator Award in Patient-Oriented Research Awards* (K24) for the support of mid-career investigators in research and mentoring; and (3) *Clinical Research Curriculum Development Awards* (K30) for curriculum development in clinical research. All three of these awards 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, the initiative specified that at least 80 K23 and 80 K24 awards would be made in each of the next 5 fiscal years to achieve a steady state of approximately 400 of each type of award. This target was chosen as a compromise between estimated needs for new researchers and the need to increase the capacity to provide this type of training. The K30 was targeted for 20 awards in FY 1999, but does not extend into future years. After the five-year initial period, the NIH will examine the continuing need for this program and will set new numerical targets if necessary. It may be possible, at that point, to manage this award without numerical targets. In that case, the NIH would manage the application rate with announcements, changes in award provisions, and a stable success rate in the same manner as other research training and career awards.

### ***Performance Assessment Approach***

#### *Basis and Data:*

Performance will be measured by the number of applications and awards in the K23 and K24 categories. NIH will use the IMPAC database to enumerate the total number of applications received and the total number of applications awarded during this time period.

#### *Validation and Verification:*

IMPAC is a comprehensive database at NIH, built and refined over many years, that covers the agency's extramural research activities. Included here are records of research contracts, records of in-process grant applications, and inter- and intra-agency agreements. The data in IMPAC is compared to accounting data maintained by the Office of Financial Management on a daily basis and there is a record of all applications and awards processed by the NIH.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Issue at least 80 awards each in the K23 and K24 categories over the course of the fiscal year.**



Target substantially met. NIH made 189 awards in the K23 category in FY 2000, out of 390 applications received. 75 K24 awards were made, out of 168 applications received.

While the K24 target was not entirely met, the substantial number of new investigators recruited into patient-oriented research by the K23 means that the overall goal is being met.

Assessment Data: The data are from NIH's IMPAC database (see the *Performance Assessment Approach* discussion earlier.)

### ***Progress Toward Goal Achievement***

Cumulatively, over FY 1999 and 2000, the number of K23 awards has been greatly larger than the level targeted: 274 awards vs. a target of 160. That for the K24 award has been slightly below: 156 awards vs. 160.

All taken together, the progress to date has clearly been successful in attracting new researchers into patient-oriented research.

### ***Next Steps***

Continue to monitor the application rates and success rates for these two new awards. If it appears that numerical goals are not being met, the policies or financial features of these awards may be altered to make the awards more attractive.

In addition, the NIH intends to conduct focus groups of new recipients of K23 support to determine if the NIH funded career development experience is expanding recipients' knowledge and skills as a researcher. A report on these focus groups will become available during FY 2001.

**Goal c) Increase the participation of under represented racial and ethnic groups, women, and individuals with disabilities in NIH training and research programs.**

### Performance Targets & Results

#### FY 2002

**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.**

*Performance to be reported in February 2003.*

#### FY 2001

- 1. Establish new paradigm for measuring the race/ethnicity of NRSA recipients to bring the NIH into compliance with OMB guidelines.**
- 2. 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.**
- 3. Implement OMB required race/ethnic data collection and reporting strategy.**

*Performance to be reported in February 2002.*

#### FY 2000

Plan action as appropriate to identify and address demographic groups for which interest in training is abnormally low or declining.

*Performance: Target met. NIH continues to actively enforce minority recruitment requirements on T32 research training grants and continues to monitor the participation of individuals from underrepresented groups.*

#### FY 1999

- 1. Prepare a report identifying the demographics of the individuals supported by the NRSA mechanisms and career award mechanisms.**

*Performance: Target not met. Programs have been developed to extract race/ethnicity data on individuals newly appointed to NIH research training grants, but the analysis has not been completed.*

- 2. 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.**

*Performance: Target met. The NPRM for 42 Part 66 (to permit part-time NSRA support and part-time payback options for individuals with pressing family obligations or disabilities) was published in the Federal Register on June 30. (This NPRM is intended particularly to respond to the needs of young women.)*

Note: FY 2000 target #1 included effort to complete the activities indicated in FY 1999 target #1 but which were incomplete in that year.

### ***Goal Background***

NIH is committed to training and supporting a research community that reflects the nation's social diversity. Accordingly, NIH supports a number of training programs specifically designed to provide support to minority graduate and postdoctoral students and to recruit them into research at all career levels. NIH also supports 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. An important aspect of these efforts is a continual monitoring of the demographics of the participants in NIH programs. This ongoing vigilance permits an assessment of the value of existing initiatives and the identification of emerging problem areas.

Of particular interest is OMB's revision of Directive 15 (for details see <http://www.whitehouse.gov/OMB/inforeg/race.pdf>) related to the collection of data on race and ethnicity. Under the new guidelines, all Federal agencies must collect information on ethnicity separately from race. Also, respondents are to be offered the option of indicating more than a single race. OMB has also offered recommendations related to the reporting of the new data. As the NIH moves toward compliance with the new guidelines, 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) will need to be modified. In addition the data entry screens for IMPAC II and the underlying data structures will have to be modified to accept the new data. Finally, reporting conventions that adjust for discontinuities in the nature of race/ethnic data will have to be designed and approved.

### ***Performance Assessment Approach***

#### *Basis and Data:*

Performance will be measured by assessing the participation of individuals of different races and ethnicity in NIH research and training programs. NIH will use the IMPAC database to enumerate the total number of applications received and the total number of applications awarded from these groups over time.

In the past, the level of response to questions about race and ethnicity has been in the 75-85 percent range. This response rate is lower than needed to obtain good statistical estimates of participation rates. The data shown in the chart further below represents the proportion of individuals from racial and ethnic groups underrepresented in biomedical sciences (Hispanic or Latino, Black or African American, American Indian or Alaska Native, Native Hawaiian or Pacific Islander) when compared to the number reporting. Also included are individuals from a small number of research training grants that specifically target underrepresented groups. Since, the collection of this information will remain voluntary, improving the level of response will

require form redesign and a better explanation of the importance of this information. Both processes are underway.

*Validation and Verification:*

IMPAC is a comprehensive management database at NIH, that has been built and refined over many years and covers the agency’s extramural research activities. Included are records of research contracts, records of in-process grant applications, and inter- and intra-agency agreements. The data in IMPAC is compared to accounting data maintained by NIH’s Office of Financial Management on a daily basis, and there is a record of all applications and awards processed by the NIH.

***FY 2000 Performance Assessment***

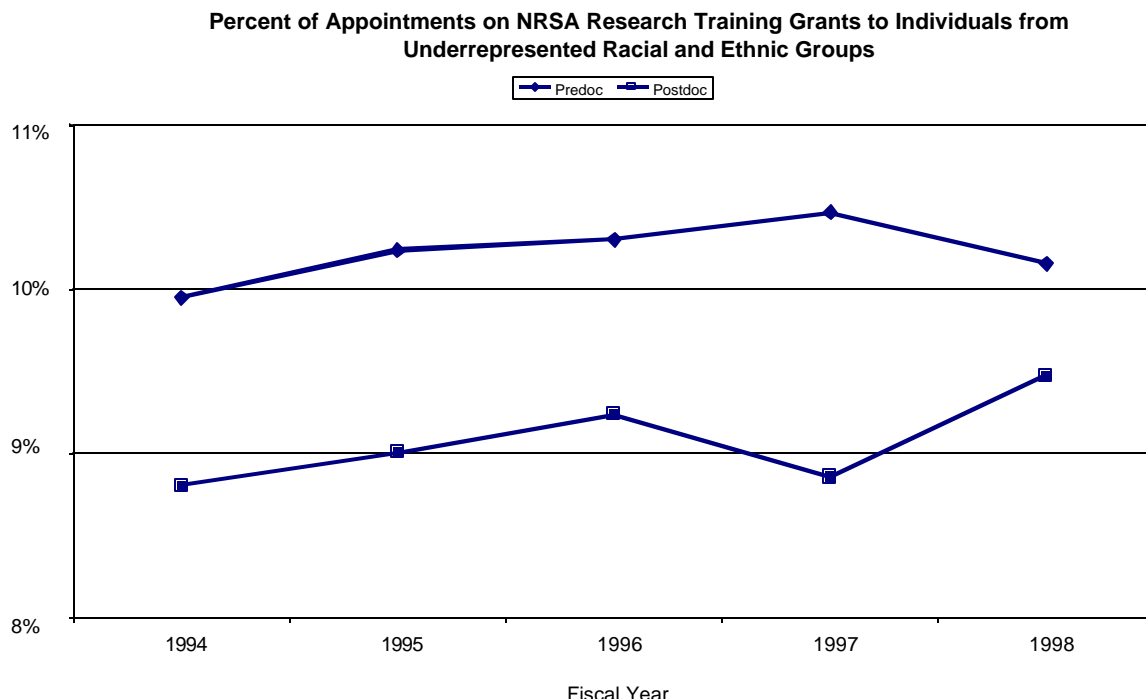
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***Discussion of FY 2000 Results***

**Target: Plan action as appropriate to identify and address demographic groups for which interest in training is abnormally low or declining.**

Target met. NIH continues to actively enforce the minority recruitment requirement on T32 research training grants and continues to monitor the participation of individuals from underrepresented groups.

As illustrated in the chart below (and discussed further in the next section), there has been a slow increase in the participation of individuals from underrepresented racial and ethnic groups in the NIH research training programs.



It needs to be noted that the most recent year reported here (FY 1998) reflects the fact that there is a delay in receiving information about appointments to research training grants. It usually takes at least two years to receive 95 percent of all such information.

Assessment Data: Data are from the IMPAC database and from reports provided by each of the NIH Institutes and Centers. The data is captured from Statement of Appointment Forms (PHS Form 2271), which are submitted to the NIH at the beginning of each training appointment. The provision of information on race or ethnicity is completely voluntary.

### ***Progress Toward Goal Achievement***

While progress remains slow, NIH continues to attract women, minorities and individuals with disability into health-related research.

Women continue to account for approximately 45% of the training pool at both the predoctoral and postdoctoral levels in the biomedical sciences. Also, women continue to make gains and account for more than 60% of the students and postdoctorates in the social and behavioral sciences.

With regard to underrepresented ethnic and racial groups, the total number of predoctoral and postdoctoral NRSA trainees and fellows in these categories ranged between 810 and 951 each year from 1994 to 1998. Over this period, 9.4 to 9.9% of all NRSA appointments at the predoctoral and postdoctoral levels have gone to individuals from groups shown to be underrepresented in the biomedical sciences (see chart below). American Indians or Alaska Natives ranged between 0.5 and 0.8%, Black or African Americans ranged between 4.4 and 4.8%, Hispanic or Latino Americans ranged between 3.7 and 4.4%, and Native Hawaiian and other Pacific Islanders ranged between 0.4 and 0.7% of all trainees and fellows who reported their race or ethnicity. These groups remain underrepresented within the pool of trainees but their participation appears to be slowly increasing.

The NIH also encourages directors of NIH research training programs to support individuals with disabilities. Support for accommodation is provided when it is needed. The NIH also supports supplements for individuals with disabilities. In FY 1999, this program supported 53 students, postdocs, or faculty members with disabilities. Information on this program can be found at <http://grants.nih.gov/training/outcomes.htm>. In addition, graduate students with disability can apply for and receive fellowship support for their graduate training.

### ***Next Steps***

NIH will continue to monitor the participation of underrepresented groups and enforce the minority recruitment policy on NRSA research training grants. NIH will also update the Statement of Appointment Form to improve the response rate to questions of race and ethnicity. The supplement programs for minority and disabled researchers will be re-announced in FY

2001. Policies for those programs are being adjusted to improve the level of support and expand the number of research grants eligible for such support. NIH will develop formal policies to allow individuals with disability to engage in research training at less than full-time when necessary.

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

### Performance Targets & Results

#### FY 2002

**Implement recommendations in the quadrennial assessment of the nation's future needs for biomedical and behavioral research scientists prepared by the National Academy of Sciences (NAS).**

*Performance to be reported in February 2003.*

#### 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*.**

*Performance to be reported in February 2002.*

#### 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 National Academy of Sciences (NAS).

*Performance: Target substantially met. The National Academy report has been received and discussions related to the development of a formal implementation plan are proceeding at the highest level of NIH.*

Note: This was a new goal in FY 2000.

### Goal Background

Every four years the NIH engages the Office of Scientific and Engineering Personnel of the National Research Council, National Academy of Sciences in an study of future needs for research personnel in health related research. This periodic analysis is required by Section 489 of the Public Health Service Act (P.L. 93-348). The associated report, published every four years, is prepared by an external panel (Committee on National Needs for Biomedical and Behavioral Research Personnel) of the National Research Council.

The latest edition of this report was issued on August 29, 2000. Entitled *Addressing the Nation's Changing Need for Biomedical and Behavioral Scientists*, the report is available on NIH's Website at [http://grants.nih.gov/training/nas\\_report/index.htm](http://grants.nih.gov/training/nas_report/index.htm).

The report contains a number of recommendations about the size and nature of the NIH research training and career development programs. NIH will analyze these recommendations and

develop appropriate implementation plans, which will be reflected in future GPRA targets and goals.

### ***Performance Assessment Approach***

#### *Basis and Data:*

Achievement will be gauged by progress against the milestones established by the listed targets

It is current expected that implementation of the recommendations will be phased-in over the next several years. NIH will formally communicate the report and associated recommendations to the Congress (as required by law).

#### *Validation and Verification:*

NIH's decisions and actions in this realm will be a part of the public record.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Respond to the quadrennial assessment of the nation's future need for biomedical and behavioral research scientists issued on August 29, 2000 by the National Academy of Sciences (NAS).**

Target substantially met. The NAS report has been received and discussions related to the development of a formal implementation plan are proceeding at the highest levels of NIH.

NIH contracted with the National Academy to conduct a study on research personnel needs, as required by Section 489 of the Public Health Service Act. NIH received the report *Addressing the Nation's Changing Needs for Biomedical and Behavioral Scientists* on August 29, 2000.

Although no formal implementation plan has been issued, there is high-level agreement that the NIH should issue a statement of principles related to the education and training of graduate students and postdoctorates in life sciences. In addition, there is agreement that NRSA stipends should be increased and that NIH should begin collecting data on students and postdoctorates supported by NIH research grants. A formal response from NIH to this report is expected within the next few months and may generate new implementation targets.

Assessment Data: The National Academy's report can be viewed at <http://grants.nih.gov/training/outcomes.htm>.



***Progress Toward Goal Achievement***

NIH has now received the congressionally-mandated study. NIH is currently in the process of developing a formal response and related implementation plan.

***Next Steps***

The most important next steps include achieving final agreement on an implementation approach and issuing a policy statement in the NIH *Guide for Grants and Contracts*. Future targets could include development of a document on the principles associated with the use of federal research funds to support the career development of graduate students and postdoctorates. They might also involve development of a formal plan to begin to collect identifying information on graduate students and postdoctorates supported by NIH research grants.

**Goal e) Expand capabilities for electronic administration of research training and career development activities.**

### Performance Targets & Results

#### FY 2002

1. Nearly all training appointments are received electronically.
2. At least 50% of all termination notices are received electronically.
3. Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies.

*Performance to be reported in February 2003.*

#### FY 2001

1. At least 50% of all training appointments received electronically.
2. All electronically received appointment information is used to establish trainee appointment records and professional profiles within the IMPAC II system.

*Performance to be reported in February 2002.*

#### FY 2000

1. Increase by 40% over the 1999 number of trainee appointment forms received electronically.

*Performance: Target not met. Work is still underway as we adapt to changing technology, finalize the resource allocation processes, and address the need for compatibility with other Federal systems.*

2. 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.

*Performance: Target not met. Work is still underway as we adapt to changing technology, finalize the resource allocation processes, and address the need for compatibility with other Federal systems.*

3. Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies.

*Performance: Target not met. The overall approach to future evaluations of the NIH research training programs will be very dependent on the availability of Web-based appointment data. Since this data is not yet being collected via X-Train it is premature to engage in the development of long-term evaluation plans.*

Notes: This was a new goal in FY 2000. FY 2001 targets #1 and #2 and FY 2002 target #3 incorporate the necessary adjustments for the incomplete FY 2000 targets.

### ***Goal Background***

Organizations receiving NRSA institutional training grants are required to report the appointment of trainees supported under the grant. To facilitate this reporting, NIH is developing, as part of its electronic research administration system, a Web-based interface that permits the electronic submission of trainee appointment and termination information. This electronic system will improve the ease of data entry and processing, in addition to improving the quality of data. The specific features of this system are still in the development stage, but will be referred to collectively as the Electronic Trainee Activities System (X-Train). The X-Train utility will reside on the NIH Commons (see Grants and Administration Goal c).

During FY 2000 little progress was made to improve the capabilities of X-Train for electronic receipt of appointment and termination information. Based on information from IMPAC staff, the primary barrier was integration of the electronic appointment information with the Professional Profile. When completed, the Professional Profile will serve as a repository of biographical information on all individuals who have an affiliation with the NIH either as principal investigators, key personnel, trainees, fellows, and career award recipients. By keeping encouraging all affiliated scientists to keep their Web-based biographical information up to date, the NIH will be able to track the effect of training support on career outcomes. The database will indicate advancement to new positions, publications, appointment to advisory groups, and receipt of research project support.

In 1997, the NIH established a precursor system to X-Train. Using that system, the NIH received 614 trainee appointment forms electronically in 1997. In 1998, more than 1,029 forms were received electronically for a 68 percent increase over the previous year. Beginning in FY 2001, X-Train should completely replace the precursor system and will be initially tested by 15 Federal Demonstration Partnership institutions. It is expected that this interface will be fully operational by the end of FY 2002. A link to the future X-Train system is currently available on the NIH Commons Web Page at <https://www-commons.cit.nih.gov/>.

These new capabilities will improve and streamline the processing of training and career award data and greatly expand career tracking capabilities. Access to richer data on training experiences and career outcomes will permit NIH to undertake more comprehensive and informed evaluations of its training programs. It will also permit matching the performance of former trainees and fellows to specific characteristics of their training programs to enhance the quality of those programs. A more efficient and effective research training program should enable the NIH to better respond to the constantly changing national needs and priorities for research training.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

Data on the number of appointment forms received will be based on information from the IMPAC data system.

All electronic appointment forms received via X-Train will establish a professional profile that will be used in the future for tracking career outcomes. Each electronic form received is held in a temporary database until the contents are reviewed and approved by the NIH official responsible for the training grant. At that point, the information is loaded into the IMPAC II management information system.

*Validation and Verification:*

IMPAC II is a comprehensive, relational database, built that covers and documents the agency's extramural research activities. Enhancements to the IMPAC II are ongoing and are described in previous sections.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

#### **Target 1: Increase by 40% over the 1999 number of trainee appointment forms received electronically.**

Target not met. Work is still underway as we adapt to changing technology and address the need for compatibility with other Federal systems. NIH continues to receive electronic appointment forms through the system that preceded X-Train.

In FY 1999, 7.4 percent of all appointment information was received electronically using the precursor system to X-Train. In FY 2000, 9.5 percent of all appointments to research training grants used this system. The expected deployment of the Web-based X-Train System did not occur in FY 2000 because of budgetary problems that delayed the integration of information with the Professional Profile.

Until these problems are resolved, X-Train will not be released for use by the extramural research community. As a next step, the management of the NIH Electronic Research Administration (ERA) effort has been restructured to emphasize the identification of user requirements and establish clear funding priorities. Implementation of X-Train in FY 2001 remains a high priority.

Assessment Data: The status information comes from NIH staff responsible for the ERA. The current priorities for the entire ERA effort are discussed at <http://impac2.nih.gov/pm/pm.htm>.

#### **Target 2: 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.**

Target not met. Web-based appointment data is not yet being collected via X-Train -- or maintained by individual trainees, fellows, and career awardees.

Progress on the development of X-Train and external access to NIH Person Database information has been delayed because of a lack of budgetary resources. A restructuring of the management of the ERA effort took place in FY 2000, emphasizing the establishment of user requirements and funding priorities.

The problems with the integration of X-Train and the NIH Persons Database have been well characterized. These are expected to be resolved in FY 2001.

Assessment Data: The status information comes from NIH staff responsible for the ERA. The current priorities for the entire ERA effort are discussed at <http://impac2.nih.gov/pm/pm.htm>.

**Target 3: Develop a plan for ongoing evaluations of NIH research training programs as well as a plan for periodic, comprehensive career outcome studies.**

Target not met. The overall approach to future evaluations of the NIH research training programs will be very dependent on the availability of Web-based appointment data. Since this data is not yet being collected via X-Train it is premature to engage in the development of long-term evaluation plans.

Progress on the development of X-Train and external access to NIH Person Database information has been delayed. A restructuring of the management of the ERA effort took place in FY 2000, emphasizing the establishment of user requirements and funding priorities. It is expected that a precursor version of X-Train will now be available before the end of FY 2001 and a fully integrated version should be ready by the end of FY 2002. Once these systems are in place and are fully integrated with the Professional Profile, the use of this data will supplant sources of data historically used for career outcome studies.

Assessment Data: The status information comes from NIH staff responsible for the ERA. The current priorities for the entire ERA effort are discussed at <http://impac2.nih.gov/pm/pm.htm>.

***Progress Toward Goal Achievement***

Progress on this goal has been slower than expected, due to the introduction of new technology and attendant costs. However, with the infusion of support given to this project, X-Train remains a high priority.

***Next Steps***

Monitor the development and implementation of the X-Train and Professional Profile modules in FY 2001. With the commitment of additional resources, the quality of information in this career tracking database will be enhanced. The deployment of X-Train remains a very high priority item, and continued inclusion in the eRA process is expected to permit this aspect of the overall project to be completed.

**Goal f) Improve the capabilities for career outcome tracking for NIH training and career development programs.**

### Performance Targets & Results

#### FY 2002

**Develop the second version of X-Train as source of information on trainees. Use information from X-Train to establish a professional profile for all trainees. Use the professional profile as a source of long-term career tracking information.**

*Performance to be reported in February 2003.*

#### FY 2001

- 1. Complete a report on career outcomes of recipients of NIH extramural postdoctoral research training support.**
- 2. Conduct early evaluation of the K23 program based on focus groups composed of recipients.**

*Performance to be reported in February 2002.*

#### FY 2000

1. Initiate preliminary work on the long-term tracking database.

*Performance: Target not met. The NIH Person Database has not yet been established as a source for long-term tracking information.*

2. Complete a report on career outcomes of recipients of NIH extramural predoctoral research training support.\*

*Performance: Target met. The report, The Early Careers Progress of NRSA Predoctoral Trainees and Fellows has been completed.*

#### FY 1999

1. Complete an evaluation study of NIH pre- and post-doctoral training programs based on existing data.

*Performance: Target not met. A draft report of the NRSA Predoctoral Training Evaluation Study The Early Career Outcomes of NRSA Predoctoral Trainees and Fellows, Office of Extramural Research, has been completed and made available. Data sets for the postdoctoral study have been compiled but not analyzed.*

2. Add training activities functions to the NIH Commons.

*Performance: Target not met. The X-Train software has been available for internal testing for several months, but due to problems with related functions of the Commons, such as the Personal Profile System, X-Train is not yet operational.*

Notes: FY 2001 Target #1 and FY 2000 Target #2 reflect the revised completion schedule for those aspects of FY 1999 Target #1 that were not complete at the close of the fiscal year.

\*FY 2000 Target #2 was set but inadvertently left off as a revised final target in the February 2000 version of the agency's Annual Performance Plan.

### ***Goal Background***

NIH recognizes the importance of developing and managing its training programs based on sound knowledge about their ongoing effectiveness. Towards this end, the agency has initiated a comprehensive evaluation of the National Research Service Award (NRSA) programs for predoctoral and postdoctoral research training. This effort examines program effectiveness by determining how many recipients of this training support 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. All of these outcomes are related to the overall goal of training and maintaining a population of highly trained individuals capable of carrying out the nation's biomedical and behavioral research mission.

In response to the 1994 NAS Report, *Meeting the Nation's Needs for Biomedical and Behavioral Personnel*, NIH established a staff committee and launched a comprehensive career outcome study which is not completely finished. The original plan incorporated three different analytical components: (i) Complete an assessment of career outcomes based on existing data sources and the characteristics of former NRSA trainees and fellows. The career outcomes of NRSA recipients would then be compared to those of individuals in selected comparison groups. (ii) Conduct a sample survey of former NRSA recipients and comparison group, to identify specific and non-academic outcomes as an assessment of the impact of program elements. (iii) Establish a long-term career tracking mechanism for NRSA-supported individuals, to gather systematic longitudinal data on the relationships between program processes (e.g., duration, type of support) and outcomes. Subsequent to the initiation of these evaluation studies, the NIH Committee on Research Training Assessment (CORTA), determined that the information within the existing National Science Foundation (NSF) Survey of Doctoral Recipients (SDR) was sufficiently robust to obviate the need for a separate survey. The Predoctoral segment of the NRSA career outcome study is finished and should be published in an electronic format by the end of September, 2000.

In FY 2001, the NIH expects to complete the postdoctoral segment of the NRSA career outcome study and to conduct an early assessment of the effectiveness of the K23 program (described earlier). This assessment will be carried out using focus groups of recipients and will attempt to identify those dimensions of these career development experiences that are related to successful career outcomes. This informal study could help shape future review criteria and award monitoring. It may also be useful in establishing parameters for future data collection efforts. The long-term tracking effort, described earlier as X-Train should also be implemented in FY 2001. By 2002, it is hoped that tracking will be extended to predoctoral and postdoctoral research assistants so that all recipients of NIH support for training will provide identifying information and information related to their post-award careers.

### ***Performance Assessment Approach***

#### *Basis and Data:*

FY 2002 -- Once the X-Train system is completed, every appointment received will establish a professional profile. At that point, the NIH will begin encouraging all former trainees and fellows to update their professional profile on a regular basis in order to collect current information on publications, awards, and employment. This information will constitute the heart of the long-term tracking database and will permit an assessment of the career advancement and productivity of former recipients of NRSA support.

FY 2001 -- NIH has started a comprehensive analysis of the career outcomes of NRSA postdoctoral research training support. The career outcomes of individuals who have received 9 or more months of NRSA research training support will be compared to individuals who have expressed an interest in obtaining postdoctoral training at the time of the doctorate as recorded in the Doctorate Records File. Career outcomes of NRSA recipients will also be compared to individuals who've received other types of NIH postdoctoral support. The outcomes examined will include application for and receipt of NIH and NSF research grants, publication and citation counts, and indicators of research involvement. This information is obtained by matching records with other national data sets.

#### *Validation and Verification:*

FY 2002 -- All personal data recorded in the professional profile will be based on information provided and verified by the individual. At the time an individual adds data to his or her personal profile, he or she will be asked to provide assurance that the information is correct. Information on specific NIH awards in the professional profile will be cross-checked and verified using other NIH records. For example, information on publications can be verified by links to the NIH MEDLARS system.

FY 2001 -- Data will be based on records in the IMPAC database and are compared to information in other national databases including the Survey of Doctoral Recipients, the Survey of Earned Doctorates, MEDLARS, the Faculty Roster System, and the Institute of Scientific Information Database. The analysis of career outcomes will include the establishment of statistically valid probability samples and appropriate weighting of those samples. An established oversight committee will select the methodology and the report will undergo rigorous peer review prior to publication.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

##### **Target 1: Initiate preliminary work on the long-term tracking database.**

Target not met. The NIH Person Database (Professional Profile) has not yet been established as a source for long-term career tracking information.



Management of the Electronic Research Administration (ERA) was restructured in FY 2000, emphasizing establishment of user requirements and funding priorities. X-Train and the Person Database (Professional Profile) are high priority items within the task list of ERA items but are not scheduled for deployment until FY 2002. This database will serve as the career outcome tracking database in the future.

Assessment Data: The status information comes from NIH staff responsible for the ERA. The current priorities for the entire ERA effort are discussed at <http://impac2.nih.gov/pm/pm.htm>.

**Target 2: Complete a report on career outcomes of recipients of NIH extramural predoctoral research training support.**

Target met. The report, *The Early Career Progress of NRSA Predoctoral Trainees and Fellows* has been completed. DHHS approval for printing has been granted and printing will be initiated in May 2001.

The report shows that individuals who've received at least 9 months of NRSA predoctoral training support are more likely to apply for and receive NIH fellowships and research grants and are more likely to obtain faculty positions at prestigious universities when compared to their colleagues without NRSA support. NRSA recipients also publish more papers, and those papers are cited more frequently.

This is the first comprehensive evaluation of the NRSA programs since 1985. It demonstrates that this program continues to enhance the careers of recipients.

Assessment Data: Data for the report was obtained from NIH data files including the Trainee Fellow File, the Consolidated Grant Applicant File, and the Master Index. Information in these files has been matched to and verified by information in the NSF/NIH Survey of Earned Doctorates and the Survey of Doctoral Recipients. Information on publications and citations was obtained from the Institute of Scientific Information.

***Progress Toward Goal Achievement***

Long-term career tracking using the Person database and X-Train have not been realized. Structural problems encountered with the NIH Commons and the professional profile will require substantial redesign.

The second version of the Commons and an updated professional profile should be finished by the end of FY 2001. It is expected this will permit deployment of X-Train and also enable the professional profile as a long-term tracking database sometime in FY 2002.

Nonetheless, the use of matching algorithms across the existing databases listed in the Target 2 discussion just above is still possible. This approach has permitted completion of a

comprehensive career outcome study on former recipients of NRSA predoctoral training support. A similar study of individuals with postdoctoral training support is underway.

***Next Steps***

In FY 2002, the X-Train system and the access system for the NIH Person database (Professional Profile) should be deployed and tested. We also expect that a career outcome report on recipients of postdoctoral training support will be completed in FY 2001. Assessment of the need for evaluation support to improve the capabilities and the quality of data in the Professional Profile will be completed.

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### 2.3 Research Facilities Program

<b>GPRR Research Facilities Program</b>				
<b>FY 2002 President's Budget Request</b> (dollars in thousands)	<b>FY 1999 Actual</b>	<b>FY 2000 Actual</b>	<b>FY 2001 Estimate</b>	<b>FY 2002 Estimate</b>
	<b>\$239,343</b>	<b>\$251,747</b>	<b>\$240,799</b>	<b>\$422,204</b>
<b>Major Functional Areas</b>	<b>Intramural Modernization and Improvements</b> – 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.			
	<b>Extramural Assistance</b> -- Assist in the construction and modernization of non-federal facilities at academic institutions and other centers of research excellence to enhance their ability to begin new and continue to conduct high-quality research.			

#### 2.3.1 Program Description, Context, and Summary of Performance

**Program Description and Context.** The Research Facilities Program addresses NIH's long-term goal to "secure facilities for research that are modern, efficient and safe." NIH's activities and resources in this Core Program area are directed along two principal lines: *Intramural Modernization and Improvements* and *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 medical and behavioral research. In addition to the over 70 buildings located on the main NIH campus in Bethesda, Maryland and the National Institute of Environmental Health Science (NIEHS) campus in Research Triangle Park, North Carolina, the NIH 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; the Rocky Mountain Laboratory in Hamilton, Montana, and New Iberia, Louisiana.

The original construction of these buildings and facilities spans a period of more than 60 years, dating back to the June 1936 legislation which authorized Building 1 on the Bethesda campus. As a result, the NIH is now contending with an aging physical plant, and 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 other factors lead to facility obsolescence and the need for modernization and replacement of facilities.

Facilities revitalization goals are established through a process which annually evaluates building and facility program needs. This effort culminates in the NIH Buildings and Space Plan, the Agency Capital Plan, and a Five Year Development Program. Other tools used to plan, program, and budget for capital assets include: facility assessments and surveys, engineering studies, technologically driven initiatives and advancements, changes in regulatory requirements, and the recommendations of the approved NIH Facilities Master Plan.

The Buildings and Facilities program (B&F) is composed of five major areas: Essential Safety and Health Improvements, Repair and Improvements, New Construction, Renovations, and Building Equipment/System Upgrades. The focus of the B&F is to provide facilities which are 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 research needs.

*Extramural Assistance* -- NIH is authorized under the Public Health Service Act 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 medical and behavioral research and research training. Such grants to extramural research facilities are awarded competitively, with grantee institutions required to obtain matching funds for the specific project awarded.

The NIH collaborates with the National Science Foundation to assess the condition of existing facilities and identify needs for new and refurbished research facilities nationwide. These studies provide the major source of objective data for national research infrastructure policy and planning needs. When particular needs are identified, the NIH offers competitive funding opportunities. This support encompasses “bricks & mortar” modernization and replacement of existing research facilities -- all of which result in new capabilities that can open areas of innovative research activity.

**Summary of Performance.** Comprehensive summary tables covering all the goals and targets in this program appear at the outset of each functional area discussion. Please refer to the following pages:

Intramural Modernization and Improvements.....	324
Extramural Assistance.....	352

## **2.3.2 Goal-by-Goal Presentation of Performance Goals and Results**

### **2.3.2.1 Intramural Modernization and Improvements**

NIH's Intramural Modernization and Improvements program manages NIH's capital assets and is integral to the success of the intramural research program in achieving its research goals, as well as the national health goals established by the Department of Health and Human Services. The IMIP facilitates development of NIH's annual facility planning, programming, budgeting and construction execution strategies that include the energy reduction objectives of the National Energy Conservation Policy Act and Executive Order 13123 and other facility management initiatives.

The Program is the product of a systematic process of interaction between the facility planning, programming, design and construction components of the NIH and the various Institutes and Centers on NIH campuses. 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. Building and Facilities (B&F) program requirements are reviewed and prioritized by a cross-organization Facilities Planning Advisory Committee (FPAC) that culminates in the NIH 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, or the unique operating requirements and age of the facilities in NIH's inventory. Included are: (1) essential safety and health improvements, (2) new construction, (3) renovations, (4) equipment and systems, (5) repair and improvements.

Under the B&F program, new facilities are programmed or existing facilities are modernized or replaced when this is the most viable option to support current or emerging research and technological advancements in the IRP. Facilities are renovated or upgraded on a case-by-case basis to create an environment that can support today's complex, unique and sophisticated research requirements when new construction is not the most feasible alternative.

NIH faces a number of major challenges that can slow the progress of the intramural research effort due to the age of the agency's facility inventory. The primary areas of concern are: (1) the inability to continue to provide state-of-the-art research space in an aging facility inventory; (2) the inability to support technological advancements in current space and its detrimental impact on 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.

The major FY2002 goals and objectives of the B&F program which assist the intramural research program in satisfying its research goals are as follows:

- Ensure 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.
- Ensure facilities comply with research and accreditation guidelines that can sustain peer reviews and reflect NIH's commitment to excellence as the world leader in bio-medical research.
- Continue facility renovation, improvement and new construction projects in response to current and emerging research requirements, and technological advancements.
- Enhance operations and utilization of intramural facilities and the availability and reliability of campus-wide utility distribution systems and supporting equipment.
- Improve efficiency and effectiveness of the NIH Real Property Inventory.

The performance goals for this program area encompass facility initiatives and activities to improve NIH's ability to achieve its research goals through the comprehensive facility revitalization effort that is integral to the B&F program.

New construction is currently underway to promote collaborative structural, molecular and other biological research in the Louis Stokes Laboratories and to facilitate state-of-the-art clinical research in the new Mark O. Hatfield Clinical Research Center.

Planning and design activities are underway to provide a consolidated Central Vivarium/Animal Research Center to replace inadequate and inefficient animal facilities that can no longer satisfy the needs of the research community and are a drain on limited resources which focus on the maintenance and repair of NIH's aging facility inventory.

**Performance Goals Summary Table – Intramural Modernization and Improvements**

Performance Goals	FY Targets	Actual Performance	Details
<p><b>a) Improve the operating conditions and environment of intramural facilities and the availability and reliability of NIH utility distribution systems to support Intramural Research Program.</b></p>	<p><b>FY 2002</b>                      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.</p> <p><b>FY 2001</b>                      1. Continue projects to correct building and utility system deficiencies, repair interior and exterior of buildings, and repair off-campus facilities.                       2. Complete construction of campus-wide utility distribution systems, renovation and modernization of existing boilers, and the extension of the power plant to provide the necessary equipment to support the heating and cooling requirements of facilities on the NIH Bethesda campus.</p> <p><b>FY 2000</b>                      1. Continue projects to correct utility system deficiencies, repair interior and exterior of buildings, and repair off-campus 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.</p> <p><b>FY 1999</b>                      1. Complete projects in the following backlog categories: campus utilities, exterior and interior building repairs, roof repairs, and off-campus facility repairs.                       2. Complete construction of the Utility Tunnel Extension Project and the relocation of underground utilities to support the Power Plant Extension</p>	<p><b>FY 2002</b>                      To be reported in Feb. 2003.</p> <p><b>FY 2001</b>                      To be reported in Feb. 2002.</p> <p><b>FY 2000</b>                      Target substantially met. 93% of intended FY 2000 repairs were completed.                       Target significantly exceeded. 100% of the site utilities were completed.</p> <p><b>FY 1999</b>                      Target substantially met. Most, but not all, of the backlog projects were completed in FY 1999.                       Target substantially met. The Utility Tunnel project was completed as planned. The Power Plant project was</p>	<p>Page 327</p>



Performance Goals	FY Targets	Actual Performance	Details
	Project.	98% complete.	
<b>b) Complete the Dale and Betty Bumpers Vaccine Research Center.</b>	<p><b>FY 2000</b> Complete construction of the Dale and Betty Bumpers Vaccine Research Center.</p> <p><b>FY 1999</b> 1. Complete design and begin construction of the new vaccine research center.  2. Provide interim laboratory space for vaccine research.</p>	<p><b>FY 2000</b> Target met. Construction of the VRC was completed as scheduled.</p> <p><b>FY 1999</b> Target met. Design completed and construction started.  Target met. Interim laboratory space was provided.</p>	Page 331
<b>c) Complete the Louis Stokes Laboratories Building.</b>	<p><b>FY 2001</b> Complete construction.</p> <p><b>FY 2000</b> Complete 95% of construction.</p> <p><b>FY 1999</b> Complete 65% of construction.</p>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target substantially met. 90% of construction completed.</p> <p><b>FY 1999</b> Target substantially met. 56% of construction completed.</p>	Page 334
<b>d) Complete the Mark O. Hatfield Clinical Research Center.</b>	<p><b>FY 2002</b> Complete 95 % of construction.</p> <p><b>FY 2001</b> Complete 50 % of construction.</p> <p><b>FY 2000</b> Complete the superstructure and exterior wall system.</p> <p><b>FY 1999</b> Complete the design and the first phase of site work.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target not met. 65% of the superstructure was completed.</p> <p><b>FY 1999</b> Target substantially met. 100% of site work and 95% of the design work completed.</p>	Page 338
<b>e) Complete the Warren Grant Magnuson Clinical Center Revitalization Program.</b>	<p><b>FY 2002</b> Start design for the interim renovations and for Phase I of the Building 10 Revitalization Program.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p>	Page 342
<b>f) Maintain the quality of the NIH Animal Care Program and</b>	<p><b>FY 2002</b> Award a construction contract for the sitework and foundation for the facility as</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p>	Page 344

Performance Goals	FY Targets	Actual Performance	Details
<p><b>construct a Central Vivarium/Animal Research Center (ARC).</b></p>	<p>design is being completed.</p> <p><b>FY 2001</b> Award a developer manager contract, select the design architect-engineering firm and complete the schematic design.</p> <p><b>FY 2000</b> Begin design for the Central Vivarium/ARC sitework and foundation and the programming effort for the facility.</p> <p><b>FY 1999</b> Receive accreditation from the Association of Assessment and Accreditation of Laboratory Animal Care International.</p>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p> <p><b>FY 2000</b> Target not met. Programming discussions underway. But progress not sufficient to begin design work.</p> <p><b>FY 1999</b> Target met. AAALAC accreditation received.</p>	
<p><b>g) Construct the John Edward Porter Neuroscience Research Center on the NIH Bethesda Campus</b></p>	<p><b>FY 2002</b> Start construction of the 200,000 GSF facility on the Building 35 site.</p> <p><b>FY 2001</b> Assemble project team and begin demolition of Building 35.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002.</p>	<p>Page 347</p>
<p><b>h) Utilize a systematic process to manage and account for NIH's Real Property Inventory</b></p>	<p><b>FY 2001</b></p> <ol style="list-style-type: none"> <li>1. Provide Foundation Information for Real Property Management (FIRM) online monitoring and reporting capabilities at the desk of each stakeholder involved with real property management.</li> <li>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.</li> <li>3. 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.</li> </ol>	<p><b>FY 2001</b> To be reported in Feb. 2002.</p>	<p>Page 349</p>

## 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.**

### Performance Targets & Results

#### FY 2002

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.

*Performance to be reported in February 2003.*

#### FY 2001

1. Continue projects to correct building and utility system deficiencies, repair the interior and exterior of buildings, and repair off-campus 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.

*Performance to be reported in February 2002.*

#### FY 2000

1. Continue projects to correct utility system deficiencies, repair the interior and exterior of buildings, and repair off-campus 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.

*Performance: Target substantially met. 93% of NIH's intended FY 2000 repairs to interior and exterior building systems was achieved.*

*Performance: Target significantly exceeded. All (100%) of the site utilities to support buildings in west, north, southeast, south and southwest sections of the campus were completed in FY 2000.*

#### FY 1999

1. Complete projects in the following backlog categories: campus utilities, exterior and interior building repairs, roof repairs, and off-campus facility repairs.

*Performance: Target substantially met. Most, but not all, of the FY 1999 scheduled backlog projects were completed. 100% of the off-campus facility repair and 100% of the roof repair projects. 92% of the exterior and interior repair projects, and 86% of*

<b>Performance Targets &amp; Results</b>
<i>those associated with campus utility systems were completed.</i>
<p>2. Complete construction of the Utility Tunnel Extension Project and the relocation of underground utilities to support the Power Plant Extension Project.</p> <p><i>Performance: Target substantially met. Construction of the Utility Tunnel Project reached the 100% milestone in FY 1999 as scheduled. Construction to relocate the underground utilities to support the Power Plant Expansion Project was 98% complete at the end of FY 1999.</i></p>



Note: The FY 2001 targets include adjustments for the FY 2000 targets that were incomplete as the FY ended.

### ***Goal Background***

NIH is responsible for ensuring that all modernization and improvements to intramural research facilities keep pace with research and patient care demands, rapidly changing technological advancements, and research priorities. There is an extensive backlog of deferred maintenance and repair work requirements for NIH capital assets which range in age from 20 to 40 years and are nearing their useful life expectancy. This work includes architectural, structural, mechanical, plumbing and electrical system repairs.

A systematic approach has been adopted to budget for and to accomplish reduction of the backlog. NIH strives to achieve funding levels for building and infrastructure repairs and improvements consistent with the recommendations of the National Academy of Sciences (NAS). NIH also established procedures to identify, track, monitor, and correct the numerous building deficiencies which impact NIH's ability to achieve its goals when system malfunctions occur which could result in loss of research and further delay in the ability to find cures for the world's diseases.

Unless funding is provided for capital repairs at a rate closer to what is recommended by the NAS, the amount of deferred maintenance and repair work will continue to expand, and NIH's research objectives for the 21st century could be impacted.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives

established by the November 1999 ISO9000 certification of ORS’s Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

*Validation and Verification:*

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results***

**Target 1. Continue projects to correct utility system deficiencies, repair the interior and exterior of buildings, and repair off-campus facilities.**

Target substantially met. 93 % of the intended projects were completed in FY 2000, as shown in the table below. Only earmarked projects for Campus Utilities and Exterior and Interior Building Repairs were not fully met.

<b>FY2000 Construction Projects</b>				
<b>Backlog Areas</b>	<b>Scheduled Project</b>	<b>Completed Projects</b>	<b>Projects in Progress</b>	<b>Percent Completed</b>
Campus utilities	21	20	1	95 %
Exterior and interior repairs	30	27	3	90 %
Off-campus facility repairs	4	4	0	100 %
<b>Total</b>	<b>55</b>	<b>51</b>	<b>4</b>	<b>93 %</b>

**Target 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.**

Target significantly exceeded. The site utilities to support buildings in west, north, southeast, south and southwest sections of the campus were all completed (100%) in FY 2000, exceeding the established goal of 90% by the end of the fiscal year.

Assessment Data: These assessments rely on data from ORS' management information systems, as well as from contractor's progress reports, certified invoices, and site inspections (see the *Basis and Data* and *Validation and Verification* sections above for additional details.)

### ***Progress Toward Goal Achievement***

NIH continues to improve the reliability of its aging capital assets by meeting or exceeding its targeted goals to repair interior and exterior building systems. This effort contributes to the development of an improved operating environment which enables technological advances in the treatment and cure of diseases.

In addition, NIH's success in meeting its research goals depends on the availability of reliable and adequately sized utility distribution systems that can respond to the current and emerging needs of the scientific community. Both short- and long-term utility requirements are evaluated continually through NIH's facilities planning processes. Actions are taken to strategically provide resources when and where needed. NIH's FY 2000 goals and accomplishments focused on the most pressing utility system requirements.

### ***Next Steps***

Actions are underway to complete all remaining FY 2000 targets for campus utility and exterior/interior repair projects in the second quarter of FY 2001. Also, as a broad strategy, NIH continues to evaluate the condition of its capital assets through surveys and technical studies. This information will aid in the development of future performance goals to mitigate potential impacts on NIH operations.

**Goal b) Complete the Dale and Betty Bumpers Vaccine Research Center.****Performance Targets & Results****FY 2000**

Complete construction of the Dale and Betty Bumpers VRC.

*Performance: Target met. Construction of the VRC was completed as scheduled in FY2000 within the budgeted amount of \$26.1M.*

**FY 1999**

1. Complete design and begin construction of the new vaccine research center.

*Performance: Target met. Design of the VRC was completed and construction started in September 1998.*

2. Provide interim laboratory space for vaccine research.

*Performance: Target met. Interim laboratory space was provided for vaccine research.*

Note: Construction of the VRC was initiated in response to former President Clinton's 1997 challenge to NIH and the scientific community to produce an AIDS vaccine within 10 years (see also NIH's Research Program Goal g).

**Goal Background**

The Dale and Betty Bumpers Vaccine Research Center (VRC) is a consolidated facility to support all aspects of vaccine research, including the integration of modern immunological science with detailed understanding of the pathogenesis of HIV infection, the development of immunogens and vectors, new approaches to vaccination, and the evaluation of research and treatment protocols.

The VRC is a five-story structure with approximately 7,859 gross square meters (84,600 gross square feet) of laboratory, animal care, administrative, and educational space for the NIH Intramural Program. The facility will provide an environment that can strengthen the advance of science toward a cure for AIDS and enhance treatment modalities.

The Department of Health and Human Service's concern to provide a better quality of life for Americans and the millions of people around the world infected with HIV made it imperative that this facility be provided.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives established by the November 1999 ISO9000 certification of ORS's Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

#### *Validation and Verification:*

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

#### **Target: Complete construction of the Dale and Betty Bumpers VRC.**

Target met. Construction of the VRC began as scheduled in 1998 and was completed in September 2000, meeting the established goal.

(See building photo on next page)

Assessment Data: This assessment relies on data from ORS' management information systems, as well as from contractor's progress reports, certified invoices, and site inspections (see the *Basis and Data* and *Validation and Verification* sections above for additional details.)

#### ***Progress Toward Goal Achievement***

NIH met its construction goal of providing a facility in which research could be conducted to respond to the challenge of finding a cure for AIDS. The Dale and Betty Bumpers VRC is operational, and research is taking place in pursuit of this objective.





The Dale and Betty Bumpers Vaccine Research Center, as completed.

**Goal c) Complete the Louis Stokes Laboratories Building.**

Performance Targets & Results
<p><b>FY 2001</b></p> <p><b>Complete construction.</b></p> <p style="text-align: center;"><i>Performance to be reported in February 2002.</i></p>
<p><b>FY 2000</b></p> <p>Complete 95% of the construction.</p> <p style="text-align: center;"><i>Performance: Target substantially met. Construction of the building reached the 90% phase at the end of FY 2000.</i></p>
<p><b>FY 1999</b></p> <p>Complete 65% of the construction.</p> <p style="text-align: center;"><i>Performance: Target substantially met. Construction of the Louis Stokes Laboratories building was 56.4% complete at the end of FY 1999. ( This deviation was driven by the need to make space adjustments to support current and projected research requirements. Schedule adjustments to compensate for this deviation have been incorporated into the targets for FY 2000 and 2001.)</i></p>

Notes: The FY 2001 target includes adjustments for the FY 2000 activities incomplete as the FY ended. Based on the construction contract that was awarded for this project, this facility is scheduled to be completed in FY2001 within the budgeted amount of \$93.6M.

**Goal Background**

The Louis Stokes Laboratories (Building 50) replaces various existing obsolete laboratory facilities on the Bethesda Campus. The facility as shown below, is a six-story, 24,154 gross square meter (260,000 gross square feet) consolidated research laboratory that includes laboratories, animal facilities, a nuclear magnetic resonance lab, a cryogenic electron microscope suite, special procedure areas, and associated administrative space. Various NIH Institutes and Centers -- 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 the National Heart Lung and Blood Institute -- will utilize this facility.

The facility will provide a state-of-the-art environment incorporating 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 energy savings

features not present in the obsolete facilities now used to house the various research programs scheduled to occupy the structure. The energy design features will also help toward reduction in energy consumption consistent with energy conservation objectives.

The Louis Stokes Laboratories permits consolidation of research functions now housed in various laboratory structures that can no longer meet the needs of today's research and technological advancements and will provide an environment where collaborative research can take place to potentially result in faster delivery of cures for infectious diseases and disorders.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives established by the November 1999 ISO9000 certification of ORS's Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

#### *Validation and Verification:*

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

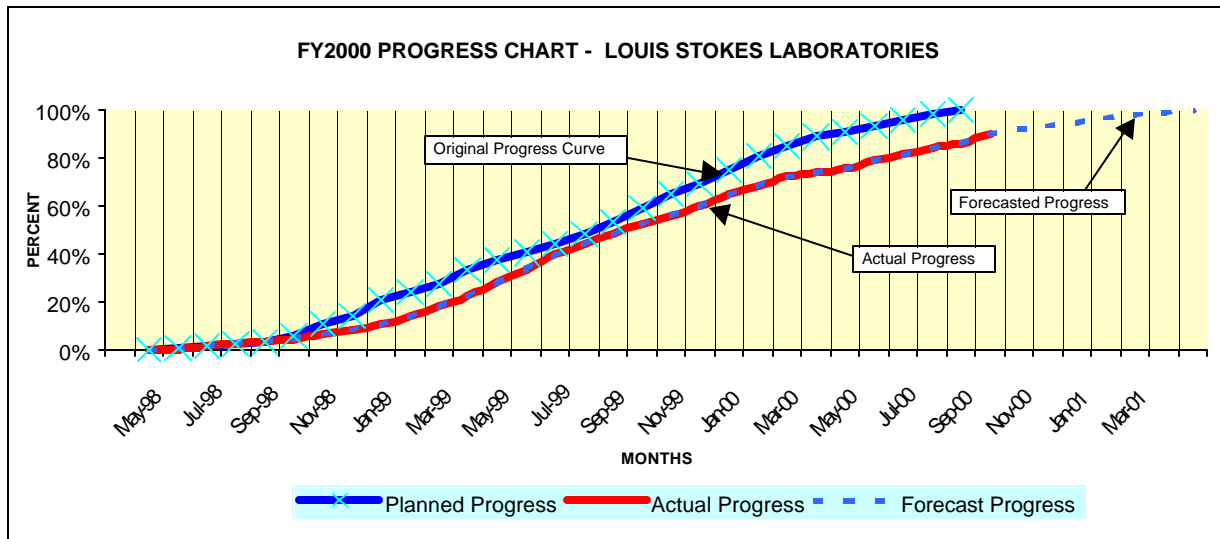
##### **Target: Complete 95% of the construction.**

Target substantially met. Construction of the Louis Stokes Laboratories (Building 50) reached the 90% phase at the end of FY 2000. This is a 5% deviation from the construction achievement level targeted for this FY.

This deviation is chiefly attributable to the essential scope changes necessary in prior years to assure that a state-of-the-art facility was provided to support research requirements. To a lesser degree, the deviation can also be traced to material and labor shortages in the construction industry.



Photo of the Louis Stokes Laboratories facility taken from the north.



Assessment Data: This assessment relies on data from ORS’ management information systems, as well as from contractor’s progress reports, certified invoices, and site inspections (see the *Basis and Data* and *Validation and Verification* sections above for additional details.)

***Progress Toward Goal Achievement***

Significant progress has been made to date complete the construction of this building. Some deviations in the planned schedule have occurred. Early programming changes to ensure the facility’s support of research needs, the booming construction industry, and material shortages

have impacted NIH's construction effort. These deviations will not, however, have a detrimental impact on research nor will they delay the existing plan to have the facility on-line in FY 2001.

*Next Steps*

Construction is now scheduled to be complete in the second quarter of FY 2001. The intended goal of having this facility on line in FY 2001 will still be achieved.

**Goal d) Complete the Mark O. Hatfield Clinical Research Center.**

Performance Targets & Results
<p><b>FY 2002</b></p> <p><b>Complete 90% of construction.</b></p> <p style="padding-left: 40px;"><i>Performance to be reported in February 2003.</i></p>
<p><b>FY 2001</b></p> <p><b>Complete 50% of construction.</b></p> <p style="padding-left: 40px;"><i>Performance to be reported in February 2002.</i></p>
<p><b>FY 2000</b></p> <p>Complete the superstructure and exterior wall system.</p> <p style="padding-left: 40px;"><i>Performance: Target not met. Construction of the building superstructure reached 65% at the end of FY 2000. Construction of the exterior wall system depends on completion of the superstructure and, accordingly, could not be started.</i></p>
<p><b>FY 1999</b></p> <p>Complete the design and first phase of site work.</p> <p style="padding-left: 40px;"><i>Performance: Target substantially met. Design of the Mark O. Hatfield CRC reached the 95% phase in FY 1999, a 5% deviation from the target. Construction for the first phase of the site work to support the facility was completed on schedule in the 2<sup>nd</sup> quarter of FY 1999 (in January 1999).</i></p>

Notes: The FY 2001 and 2002 targets incorporate adjustments for the building schedule deviations experienced in FY 2000. Based on the construction contract that was awarded for this project, this facility is scheduled to be completed in FY2003 within the budgeted amount of \$360M.

***Goal Background***

The 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 a new heart of the intramural research program, where cutting edge clinical research can take place to transfer basic science discoveries into clinical applications that respond to the National Health goals of the Department of Health and Human Services and to the strategic research goals of each Institute.

The CRC resulted from a congressional review of the importance of NIH's intramural research and the role clinical research plays in the success of its mission. Analysis of the condition and

the adequacy of the existing Warren Grant Magnuson Clinical Center (WGMCC) Building 10 in light of today's state-of-the-art and technologically adaptive and sensitive environments, resulted in recommendations that actions be taken to site the new CRC in close proximity to the existing structure. The photo below shows the new CRC in smaller profile in the foreground, and the existing WGMCC, the higher structure in the background.

The new CRC will provide an opportunity for appropriate, adaptive reuse of the existing WGMCC, to further support and advance the strategic research goals of the Department and NIH.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives established by the November 1999 ISO9000 certification of ORS's Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

#### *Validation and Verification:*

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.

### ***FY 2000 Performance Assessment***

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#### ***Discussion of FY 2000 Results***

**Target: Complete the superstructure and exterior wall system.**

Target not met. Construction of the building superstructure reached the 65 % phase at the end of FY 2000.

This 35% deviation resulted from delays in construction of the building foundation, which delayed starting and, ultimately, completing construction of the superstructure. Construction of the exterior wall system is dependent upon the superstructure work, which as indicated did not start in FY 2000 as originally planned.



Note: The construction site for the new CRC is shown in the foreground. The existing hospital is in the background.

Assessment Data: This assessment relies on data from ORS' management information systems, as well as from contractor's progress reports, certified invoices, and site inspections (see the *Basis and Data* and *Validation and Verification* sections above for additional details.)

### ***Progress Toward Goal Achievement***

This construction project progressed on schedule until unforeseen conditions were encountered during placement of the utility distribution systems on the site. This development delayed construction of the building foundation and had a ripple impact on the other interdependent construction phases.

This delay will extend completion of the superstructure until the end of FY 2001 and the start of the exterior wall system until the 3<sup>rd</sup> quarter of FY 2001. It will also require that the FY 2002



target be modified from 95% to 90% of the construction. Nevertheless, the target for completing the CRC is not anticipated to change.

***Next Steps***

NIH is working with the Developer Manager to incorporate time saving measures into the construction procedures where possible to keep the project on schedule. This includes extending the hours of construction and the use of an on-site concrete batch plant to streamline production, distribution and placement of concrete.

**Goal e) Complete the Warren Grant Magnuson Clinical Center Revitalization Program.**

**Performance Targets & Results**

**FY 2002**  
**Start design for the interim renovations and for Phase I of the Building 10 Revitalization Program.**  
*Performance to be reported in February 2003.*

Note: While originally scheduled to commence in FY 2001, this target has been reprogrammed to FY 2002. The Revitalization Program is an integrated plan that considers programmatic, logistical, and operational issues. NIH has approved the Phase I development effort and preliminary schedule and cost goals have been established to include starting the design in FY2002, starting construction by January 2004, and completing construction by January 2007 within the \$375.6M that is budgeted for Phase I. Program schedule and cost milestones will be refined upon completion of design and award of the construction contract.

***Goal Background***

The current Warren Grant Magnuson Clinical Center (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.

Routine maintenance and system repairs cannot keep pace with the vast number of deficiencies and operating inefficiencies in the facility. Construction of the new Mark O. Hatfield Clinical Research Center (CRC) provides a unique opportunity to revitalize Building 10 for adaptive re-use to support NIH’s research mission and provide an environment to facilitate achievement of the National Health Goals of the Department of Health and Human Services.

This project will reconfigure space in the existing facility to reduce over-crowded conditions, and to satisfy new research initiatives and congressional mandates. Building systems will be replaced to provide adequate capacities, to mitigate potentially unsafe environmental conditions, and to reduce maintenance and operating costs.

Success of the Building 10 Revitalization Program is dependent upon completing the interim construction efforts on various floors of the facility to house administrative and laboratory programs which will remain in Building 10 after the CRC is completed. Without this action, the NIH will not be able to provide safe, efficient and code compliant space to accommodate

programs not included in the new CRC, and those which are integral to and support the Building 10 Revitalization Program. Upon completion of the Interim Renovations, Phase I of the Building 10 Revitalization Program can begin.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives established by the November 1999 ISO9000 certification of ORS's Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

#### ***Validation and Verification:***

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.

**Goal f) Maintain the quality of the NIH Animal Care Program and construct a Central Vivarium.**

**Performance Targets & Results**

**FY 2002**

**Award a construction contract for the site work and foundation for the facility as the design is being completed.**

*Performance to be reported in February 2003.*

**FY 2001**

**Award a developer manager contract, select the design architect-engineering firm, and complete the schematic design.**

*Performance to be reported in February 2002.*

**FY 2000**

Begin design for the Central Vivarium site work and foundation, and the programming effort for the facility.

*Performance: Target not met. Facility programming discussions underway, but progress was not sufficient to begin design work.*

**FY 1999**

Receive accreditation from the Association of Assessment and Accreditation of Laboratory Animal Care International.

*Performance: Target met. AAALAC surveyors conducted a site visit of the NIH during the week of July 26, 1999. NIH received confirmation of "Deferred Continued" AAALAC accreditation based on the recommendations in this site visit.*

Note: The FY 2001 and 2002 targets incorporate adjustments for the FY 2000 activities incomplete as the FY ended. Preliminary planning efforts are underway. Our overall strategy is to begin design by the summer of 2001, complete design by the fall of 2002, start construction by the late fall/early winter of 2002, and complete construction by the summer of 2006 within the budgeted amount of \$182.8M. Schedule and cost milestones will be refined upon completion of design and award of the construction contract.

**Goal Background**

Animal Care. For the NIH Intramural Research program to fulfill its mission, it is essential that animal care facilities are accredited by the Association of Assessment and Accreditation of Laboratory Animal Care International (AAALAC). It is also crucial that the condition and environment in each facility, is suitable and adaptable to respond to emerging research demands.

Central Vivarium/Animal Research Center (ARC). The existing animal facility complex, Buildings 14/28, houses various animal species to support the research requirements for the Institutes on the Bethesda Campus. The sprawling nature of the complex, the over 40 year age of each structure, the facility conditions, and the limited capabilities of the infrastructure, and limitations imposed by the outdated design, have driven the need for significant renovations and upgrades.

It is crucial that a modern, compact, state-of-the-art Central Vivarium/ARC be provided to consolidate ongoing programs into efficient, effective, and well-functioning space to respond to current and emerging research needs for animal modeling.

The new Central Vivarium/ARC is also necessary to permit the removal of the Building 14/28 Complex to support future development of the southern quadrant of the campus consistent with the recommendations of the approved NIH Facilities Master Plan.

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 to comply with AAALAC accreditation guidelines and other applicable building codes and regulations.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives established by the November 1999 ISO9000 certification of ORS's Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

#### *Validation and Verification:*

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.

## ***FY 2000 Performance Assessment***

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### ***Discussion of FY 2000 Results***

**Target: Begin design for the Central Vivarium/ARC site work and foundation, and the programming effort for the facility.**

Target not met. Programming discussions for the facility were ongoing in FY 2000. But the progress did not reach a point that the design for the site work and foundation could begin.

Assessment Data: The assessment is based on data from ORS Management Information Systems, as well as from progress reports from the Oversight Management Committee that was established for the cradle-to-grave acquisition of this facility.

### ***Progress Toward Goal Achievement***

Completion of the programming phase for the facility is a prerequisite for developing a design and subsequently commencing the construction. The facility programming discussions, planning, and analyses now ongoing are required to ensure that this facility will reflect the emerging animal research modeling requirements. The overall goal to complete the Central Vivarium in FY 2007 remains unchanged.

### ***Next Steps***

The overall project acquisition strategy has been revised to permit procurement for the design and construction manager or developer manager to take place parallel to the facility programming effort. This is expected to minimize the impact of the FY 2000 delays. As such, no modifications to the FY 2001 and FY 2002 targets will be necessary.

<b>Goal g) Construct the John Edward Porter Neuroscience Research Center on the NIH Bethesda Campus.</b>
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Performance Targets & Results
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<b>FY 2002</b>
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<b>Start construction of the 200,000 GSF facility on the Building 35 site.</b>
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<i>Performance to be reported in February 2003.</i>
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<b>FY 2001</b>
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<b>Assemble project team and begin demolition of Building 35.</b>
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<i>Performance to be reported in February 2002.</i>
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Note: This is a new goal in FY 2001. An Integrated Project Team has been assembled and the design started in the summer of 2000. Following demolition of Building 35 in the fall of 2001, the first phase of construction will begin in the winter of 2002, and be completed by the end of 2003 within the budgeted amount of \$82.3M. Project schedule and cost goals will be refined upon completion of design and award of construction contracts.

### ***Goal Background***

NIH is committed to the creation of the John Edward Porter Neuroscience Research Center (NRC) on the Bethesda campus. Currently, the neuroscience program at NIH is dispersed among several Institutes and Centers. Scientists are segregated in one or more pre-clinical departments, removed from colleagues in clinical departments of neurology, psychiatry, neurosurgery, or anesthesiology. Elimination of these artificial barriers would create an environment where scientists focused on fundamental and clinical research could better collaborate and more quickly translate their findings into effective therapies for neurological and psychiatric disorders. Furthermore, nearly all of the space currently housing NIH neuroscience programs is not suitable for today's research standards. No major renewal in buildings housing neuroscience research has occurred in 30 years except in one structure. The major core facilities available to NIH neuroscientists have not kept pace with technological breakthroughs in genetics and imaging.

Most of the cellular and molecular neuroscience on campus is conducted in Building 36, which is located in the southwest section of the Bethesda campus. Most of the laboratories in the facility are partitioned into small modules which are separated by concrete walls that will not support collaborative research. The facility lacks shared equipment rooms, common areas for laboratory meetings, library facilities, seminar rooms, and space for ongoing scientific discourse.

The NRC will be a multi-level facility with a total of approximately 55,740 gross square meters (600,000 gross square feet) and will be constructed in phases. The facility will be designed and constructed to be sensitive to the site and the adjacent structures. The footprint of the facility is as shown on the site plan below. A collaborative environment for state-of-the-art neuroscience research with biomedical research laboratories, research support, vivarium (for both small animals and primates), lab offices, conference facilities, cafeteria, interaction areas, and public spaces will be provided in the facility. The NRC will be designed as an integral complex linked by shared public space. The initial phase of construction will be approximately 18,580 gross square meters (200,000 gross square feet) of research laboratories, vivarium for rodents, and support space located on the site of existing Building 35. The program housed in Building 36 will then be located into this new facility. Building 36 will then be demolished or modified and the remaining 37,160 gross square meters (400,000 gross square feet) will be constructed.

### ***Performance Assessment Approach***

#### *Basis and Data:*

The Office of Research Services (ORS) uses its Computerized Maintenance Management System (CMMS) and Project Information Network (PIN) system to manage and monitor the processes, procedures, objectives, and milestones established for projects to acquire new, and to modernize, replace, or enhance existing capital assets on the various NIH campuses. These tools are recognized industry standards for organizations that stress efficient and effective project management. PIN is integral to successful accomplishment of the management objectives established by the November 1999 ISO9000 certification of ORS's Design and Construction Branch (DCAB) within the Division of Engineering Services (DES).

#### *Validation and Verification:*

ISO9000 certification indicates that ORS/DES/DCAB has developed and implemented quality systems to track, monitor, verify, and validate program and project goals consistent with internationally recognized standards of operations for effectively run organizations. Both government and contract personnel play active roles in reporting and validating performance against targeted goals. The ISO9000 quality control provisions ensure the accuracy of schedule and cost data, and the progress made toward achieving established goals.



**Goal h)      Establish a systematic process to manage and account for NIH's Real Property Inventory.**

**Performance Targets & Results**

**FY 2001**

- 1. Provide FIRM online monitoring and reporting capabilities at the desk of each stakeholder involved with 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. 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.**

*Performance to be reported in February 2002.*

Note: This is a new goal FY 2001 and is expected to be completed the same year.

***Goal Background***

The NIH research mission is supported by over 200 facilities in its real property inventory. To assist in the management of its numerous facilities, NIH has embarked upon the use of a uniformly recognized real property management tool, called Foundation Information for Real Property Management (FIRM). This system provides essential accounting and reporting tools to satisfy auditing requirements and the overall mission of the NIH.

***Performance Assessment Approach***

***Basis and Data:***

Documented implementation of the pilot program for FIRM. Reports will be generated to validate the accuracy and completeness of database for each NIH facility. Evaluations will be conducted by the cognizant NIH CFO to assure that this tool is used efficiently and effectively for the NIH to conduct its business.

***Validation and Verification:***

After the pilot project has been completed there will be an assessment of the FIRM project against specific criteria to determine if the management tool has met the established goals. If the decision is made for full implementation, an implementation plan will be developed and completed. After the new process has been operating for several months, an assessment will be made to determine if the goals are being met NIH-wide. This will provide verification that the system is operating properly.

### 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 are 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 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. 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. This is dependent both on the level of funds provided by Congress and on the number of applications received that are deemed scientifically meritorious. For example, in FY 1999, 31 awards for a total of \$29.6 million were made and in FY 1998, 22 awards for a total of \$20.6 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.

NIH does not have oversight responsibility over a grantee's completion of a construction project. However, if the project is not completed within the designated timeframe, usually five years, the awarded funds revert back to the federal government. 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 Goals Summary Table – Extramural Assistance**

Performance Goals	FY Targets	Actual Performance	Details
<p><b>a) Approve construction designs that are in compliance with federal and NIH design regulations and guidelines, and with other relevant local, national, and international codes and standards.</b></p>	<p><b>FY 2002</b> Final construction design documents approved for:</p> <ol style="list-style-type: none"> <li>1. 100% of grants awarded in FY 1999</li> <li>2. 50% of grants awarded in FY 2000</li> <li>3. 25% of grants awarded in FY 2001</li> </ol> <p><b>FY 2001</b> Final construction design documents approved for:</p> <ol style="list-style-type: none"> <li>1. 100% of grants awarded in FY 1998</li> <li>2. 50% of grants awarded in FY 1999</li> <li>3. 25% of grants awarded in FY 2000</li> </ol> <p><b>FY 2000</b> Final construction design documents approved for:</p> <ol style="list-style-type: none"> <li>1. 100% of grants awarded in FY 1997</li> <li>2. 50% of grants awarded in FY 1998</li> <li>3. 25% of grants awarded in FY 1999</li> </ol> <p><b>FY 1999</b> 100% of awarded construction projects meet federal and NIH safety and architectural design regulations and are in compliance with the scope of the application.</p>	<p><b>FY 2002</b> To be reported in Feb. 2003.</p> <p><b>FY 2001</b> To be reported in Feb. 2002</p> <p><b>FY 2000</b></p> <p>Target substantially met. 86% of grants awarded.</p> <p>Target significantly exceeded. 77% of grants awarded.</p> <p>Target substantially met. 23% of grants awarded.</p> <p><b>FY 1999</b> Target partially met.</p>	<p>Page 353</p>

**Performance Goal Details - Extramural Assistance**

**Goal a) Approve construction designs that are in compliance with federal and NIH design regulations and guidelines, and with other relevant local, national, and international codes and standards.**

<b>Performance Targets &amp; Results</b>				
		Construction Design Documents Approved Fraction of Grant Awards		
		in FY(-1)	in FY(-2)	in FY(-3)
<b>FY 2002</b>	<b>Targets</b>	<b>25%</b>	<b>50%</b>	<b>100%</b>
	<i>Actual Performance</i>	<i>To be reported in February 2003</i>	<i>same</i>	<i>same</i>
<b>FY 2001</b>	<b>Targets</b>	<b>25%</b>	<b>50%</b>	<b>100%</b>
	<i>Actual Performance</i>	<i>To be reported in February 2002</i>	<i>same</i>	<i>same</i>
<b>FY 2000</b>	<b>Targets</b>	25%	50%	100%
	<i>Actual Performance</i>	23% <i>Target substantially met.</i>	77% <i>Target significantly exceeded.</i>	86% <i>Target substantially met.</i>
<b>FY 1999</b>	<b>Targets</b>	25%	50%	100%
	<i>Actual Performance</i>	23% <i>Target substantially met.</i>	77% <i>Target significantly exceeded.</i>	91% <i>Target substantially met.</i>

Notes: FY(-1), FY(-2), FY(-3) refer, respectively, to one, two, and three years before the reference fiscal year. [For example, the 2002 FY(-1) target is that 25% of the awards made in FY 2001 will have their construction designs approved by the end of FY 2002. Likewise, the 2002 FY(-3) target is that 100% of the awards made in FY 1999 will have design approval by the end of FY 2002.] This staged schedule of progress is appropriate due to the natural lag that arises in the timing of the construction design approval process (see discussion below).

This goal’s targets were given their present form in FY 2000. The original FY 1999 target differed considerably in content. The target/performance figures above for FY 1999 are imputed, based on the present form.

***Goal Background***

New and emerging biomedical research cannot be performed without well-designed facilities to develop and use cell cultures, new animal strains, therapeutics, and vaccines. To protect the public, specially designed biocontainment facilities are required to isolate, contain, and investigate infectious and other potentially hazardous agents. Furthermore, research laboratories are sophisticated and complex environments that must be specially designed to meet the

demands of experimental study, testing, and analysis, and to meet the requirements for a safe environment for personnel and the public. This double mission means that laboratories must provide levels of safety, space conditioning, and indoor air quality well above that maintained in conventional office buildings. A research laboratory's environmental conditioning system must provide protection and comfort for the occupants of the laboratory building, including those in associated non-research space.

After a construction application is awarded, but before construction may begin, another review is conducted to ensure the facilities are designed in accordance with federal and NIH design regulations and guidelines and with other related local, national, and international codes and standards. Depending on the nature of the project, the construction applicant may be required to submit up to three sets of designs: schematic design, design development, and final construction design. The applicable design documents must be approved before construction may begin.

Generally, the total project period for construction grants may be up to five years. The time between award and the approval of final construction design documents may take several years and is contingent on the grantee submitting satisfactory designs. Since awards are made towards the end of the fiscal year, the earliest approval of the final construction design documents is not possible until the next fiscal year.

As discussed earlier, the impact of NIH's extramural research facilities grants programs is directly influenced year-to-year by both the number of applications that NIH receives from the extramural research community and by the funds that the Congress makes available. Accordingly, the most meaningful way to measure the success of this program is to track the number of awards that have had their final construction designs approved.

Target percentages for the fraction of applications with final construction design approval are listed below and are based on a good management rule-of-thumb for this program.

### ***Performance Assessment Approach***

#### ***Basis and Data:***

The engineers who review the construction designs transmit an approval letter to the NIH Institute/Center when the final construction design documents are approved. Issuance of this approval letter for each grant is the primary measure of achievement for this target.

#### ***Validation and Verification:***

The final construction design approval letter for each grant is part of the formal record of the official grant files.

***FY 2000 Performance Assessment***

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***Discussion of FY 2000 Results*****Target 1. Final construction design documents approved for 100% of grants awarded in FY 1997.**

Target substantially met. Of the 22 construction awards made in FY 1997, the Division of Engineering Services (DES) has approved 19 (86%) construction design documents. Extensions have been requested by the remaining two to complete project designs and their final drawings are expected in FY 2001.

**Target 2. Final construction design documents approved for 50% of grants awarded in FY 1998.**

Target significantly exceeded. Of the 22 construction awards made in FY 1998, the Division of Engineering Services has approved 17 (77%) construction design documents. The final drawings from the five remaining institutions are expected in FY 2001.

**Target 3. Final construction design documents approved for 25% of grants awarded in FY 1999.**

Target substantially met. Of the 31 construction awards made in FY 1999, the Division of Engineering Services has approved 7 (23%) construction design documents. Several institutions have submitted their final construction design documents and approval is expected in October/November 2000. The remaining institutions are at varying stages of the construction design approval process.

Assessment Data: Issuance of a final construction design approval letter for each grant is the primary measure of target achievement. This approval letter is contained for each grant in the official grant file.

***Progress Toward Goal Achievement***

Due to the complexities involved in developing construction designs, it may take several years before the designs are submitted and approved as final. The three targets are intended to reflect the varying time frames over which grantee institutions are able to have their designs approved. Although only one the three targets was explicitly met for both FY 1999 and FY 2000, the other two targets were very close to being so. In the main, the pace of progress toward goal achievement is only slightly behind what was expected.

***Next Steps***

NCRP plans to continue conducting construction workshops to help potential grantees develop construction applications and to provide guidance on the steps required once an award is made. Having a clear understanding of the process from the beginning should give grantees a better opportunity to plan and complete the necessary steps. This should improve grantees' ability to have their construction designs approved. NCRP also communicates with the grantees when the designs are not submitted in a timely fashion. If the grantee is still behind schedule, NCRP will conduct a site visit to the institution to help expedite the design process.



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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.

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	Types of Data
<b>IMPAC</b> (Information for Management, Planning, Analysis, and Coordination)	IMPAC is a comprehensive database covering NIH's extramural research activities.	<ul style="list-style-type: none"> <li>• Records of research contracts</li> <li>• Records of in-process grant applications</li> <li>• Inter- and intra-agency agreements</li> </ul>
<b>CRISP</b> (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.	<ul style="list-style-type: none"> <li>• Abstracts and indexing terms for funded research projects</li> </ul>
<b>PRTS</b> (Purchase Request Tracking System)	A comprehensive online data system for NIH managers/administrators to initiate and track purchase requests to vendors.	<ul style="list-style-type: none"> <li>• Purchase request details</li> <li>• Sources, competition, and purchase order clearance</li> <li>• Delivery status</li> </ul>
<b>Edison</b>	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.	<ul style="list-style-type: none"> <li>• Invention disclosures</li> <li>• Patents</li> <li>• Licenses</li> <li>• Invention utilization</li> </ul>

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 ~~ia~~-scientists are the drug combinations that have ~~ean~~ 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.

***FY 2000 Assessment.*** The membership of the Assessment Working Group responsible for preparation of the FY 2000 evaluation of research outcomes reported in Part II of this document is listed in a table at the end of this appendix. An accompanying table provides a summary agenda for the main meeting day of the full Assessment Working Group.

## **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 Web site).

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 Sciences'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.

**MEMBERSHIP****GPRA Assessment Working Group of the Advisory Committee to the Director, NIH  
FY 2000 Assessment**

October 30, 2000

<p><b>Jorge L. Benach, Ph.D. (Ad Hoc)</b> State University of New York Stony Brook, NY</p> <p><b>Theodore J. Castele, M.D., FACR (COPR)</b> Fairview Park, OH</p> <p><b>Yank D. Coble, Jr., M.D. (ACD)</b> Jacksonville, FL</p> <p><b>Allen Cowley, Ph.D. (Ad Hoc)</b> Medical College of Wisconsin Milwaukee, WI</p> <p><b>Melanie Dreher, Ph.D., R.N. (COPR)</b> University of Iowa Iowa City, IA</p> <p><b>Victor J. Dzau, M.D. (ACD)</b> Brigham and Women's Hospital Boston, MA</p> <p><b>Rebecca S. Eisenberg, J.D. (ACD)</b> University of Michigan Law School Ann Arbor, MI</p> <p><b>Ralph S. Freedman, MB,Ph.D. (AdHoc)</b> The University of Texas Houston, TX</p> <p><b>Margaret Hostetter, M.D. (Ad Hoc)</b> Yale University School of Medicine New Haven, CT</p> <p><b>Ronald R. Hoy, Ph.D. (Ad Hoc)</b> Cornell University Ithaca, NY</p> <p><b>Vicki Kalabokes (COPR)</b> San Rafael, CA</p>	<p><b>Barbara B. Lackritz (COPR)</b> St. Louis, MO</p> <p><b>Joan H. Lancaster (COPR)</b> Johnson City, TN</p> <p><b>Ting-Kai Li, M.D. (ACD)</b> Indiana University School of Medicine Indianapolis, IN</p> <p><b>Richard P. Lifton, M.D., Ph.D. (Ad Hoc)</b> Yale University New Haven, CT</p> <p><b>Barbara Mason, Ph.D. (Ad Hoc)</b> University of Miami School of Medicine Miami, FL</p> <p><b>Roland McFarland (COPR)</b> Fox Broadcasting Company Beverly Hills, CA</p> <p><b>Isaac D. Montoya, Ph.D. (COPR)</b> Affiliated Systems Corporation Houston, TX</p> <p><b>William R. Morton, V.M.D. (Ad Hoc)</b> University of Washington Seattle, WA</p> <p><b>Gregory R. Mundy, M.D (Ad Hoc)</b> University of Texas Health Science Center San Antonio, TX</p> <p><b>Curtis L. Patton, Ph.D. (Ad Hoc)</b> Yale University School of Medicine New Haven, CT</p> <p><b>Daniel Porte, Jr., M.D. (Ad Hoc)</b> University of California, San Diego San Diego, CA</p>	<p><b>Jerome B. Posner, M.D. (Ad Hoc)</b> Memorial Sloan-Kettering Cancer Center New York, NY</p> <p><b>Robert Pozos, Ph.D. (Ad Hoc)</b> San Diego State University San Diego, CA</p> <p><b>Maurice F. Rabb, M.D. (COPR)</b> Chicago, IL</p> <p><b>James E. Smith, Ph.D. (Ad Hoc)</b> Wake Forest University Winston-Salem, NC</p> <p><b>P. Sarita Soni, O.D. (Ad Hoc)</b> Indiana University Bloomington, IN</p> <p><b>Arthur D. Ullian (ACD)</b> Boston, MA</p> <p><b>Thomas Vaalburg (COPR)</b> Holland, MI</p> <p><b>Myron L. Weisfeldt, M.D. (Ad Hoc)</b> Columbia University Medical School New York, NY</p> <p><b>Phillip L. Williams (ACD)</b> The Times Mirror Company Pacific Palisades, CA</p> <p><b>Douglas Q.L. Yee (COPR)</b> Morgan Stanley Dean Witter Honolulu, HI</p>
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**AGENDA****FY 2000 Assessment of NIH Research Program Outcomes****Government Performance and Results Act (GPRA)  
Working Group of the Advisory Committee to the Director, NIH**

October 30, 2000

<b>9:00</b>	<b>Opening Remarks Introductions</b>	<b>Ruth Kirschstein, M.D. Working Group Members</b>
<b>9:30</b>	<b>Overview of GPRA</b>	<b>Lana Skirboll, Ph.D.</b>
<b>9:40</b>	<b>Plenary Session: Goal A (Add to the Body of Knowledge)</b>	<b>Ting-Kai Li, M.D. Myron Weisfeldt, M.D.</b>
<b>11:30</b>	<b>Working Lunch</b>	
<b>12:00</b>	<b>Continue Plenary Session discussion of Goal A</b>	
<b>1:15</b>	<b>Concurrent Breakout Sessions: Goals B-E</b>	
	<b>Goal B: Instruments and Technologies</b>	<b>Ralph Freedman, M.B.B.Ch, Ph.D. Thomas Vaalburg</b>
	<b>Goal C: Prevention</b>	<b>Melanie Dreher, Ph.D. Curtis Patton, Ph.D.</b>
	<b>Goal D: Diagnosis</b>	<b>Allen Cowley, Ph.D. Richard Lifton, M.D.,Ph.D.</b>
	<b>Goal E: Treatment</b>	<b>Theodore Castele, M.D., FACR Victor Dzau, M.D.</b>
<b>2:45</b>	<b>Break</b>	
<b>3:00</b>	<b>Plenary Discussion of Results from Breakout Sessions, including goal attainment</b>	
<b>4:30</b>	<b>Adjourn</b>	

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## Appendix 2

### Changes and Improvements Over Previous Year

NIH's FY 2002 Annual Plan/FY 2000 Annual Report 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. Where NIH has format discretion, however, several improvements have been added this year (see below).

#### Changes and Improvements in Format

***Presentation of Targets.*** The targets for each goal are located directly below the goal and cover four fiscal years. This revision was introduced to make it easier for readers to quickly review and understand the goal, the targets related to that goal, the pace of accomplishments. This format change also enabled some modest revisions in the *Basis and Data* and *Validation/Verification* sections, which helped to reduce repetition and streamline the overall document.

***Integration of Research Outcomes Report.*** In NIH's FY 1999 annual report, the findings of the outcomes assessment panel for the Research Program Goals (a-e) were not incorporated into the plan, but were rather presented in a separate volume. In the FY 2000 annual report, this material has now been fully integrated into main body of the GPRA document.

***Integration of Other Previously Separate Sections.*** In the Research Program, in previous years, *Priority Setting*, *Grants Administration and Peer Review*, and *Management and Administration* were treated as separate areas. In the FY 2002 Annual Plan, each of these areas continues to be independently addressed, however, all three are now presented together under *Research Leadership and Administration*. In addition, in the Research Training and Career Development Program, *Training Support* and *Outreach* are now combined into a single area. In all cases, these revisions were made to link similar activities and make the document more cohesive.

***Goal Status.*** In the FY 1999 report, we not only provided descriptive outcome data, but we also provided summary labels for performance, i.e., exceeded, met, partially met, and not met. While these are not required under GPRA, we created these reporting labels to allow the reader to quickly review performance status. In FY 2000, we further refined these labels:

- ✓ *Significantly Exceeded* -- Actual performance considerably surpasses the stated target. The level of achievement is demonstrated to be particularly meritorious or significantly beyond

what was planned or expected. Where the target is numerical, this includes performance that exceeds 120% of the targeted level.

- ✓ *Met* -- Actual performance meets or even modestly exceeds the target level. The targeted level of achievement that has been reached, or even somewhat exceeded. Where the target is numerical, this includes a level of achievement that is 100-120% of the targeted value.
- ✓ *Substantially Met* -- Actual performance mostly but not completely meets the target level. The majority of work has been accomplished or major progress demonstrated in all but a few elements of the target. Where the target is numerical, this includes a level of achievement exceeding 80% of the targeted level.
- ✓ *Not Met* -- Actual performance falls well short of the target level. It has not been demonstrated that the majority of work has been accomplished or significant progress achieved. Where the target is numerical, achievement is up to 80% of the targeted level.

As required under the GPRA, targets that were “substantially met” or “not met” were accompanied with additional information regarding the actions planned to restore the intended pace of progress.

The summary for goal status for FY 1999 through FY 2002 is provided in the table below. 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	Number of Goals	Number of Targets	Level of Achievement					
			Program (# of Goals)	Number of Targets	Substantially/Significantly Exceeded	Met	Substantially Met	Not Met
1999*	49	80	Research (38)	60	12	41	3	5
			Training (5)	12	1	6	2	3
			Facilities (6)	8	0	3	4	1
2000	44	83	Research (32)	64	16	32	8	8
			Training (6)	10	0	3	3	4
			Facilities (6)	9	2	1	4	2
2001	38	86	Research (25)	63				
			Training (6)	11				
			Facilities (7)	12				
2002	34	66	Research (22)	48				
			Training (6)	10				
			Facilities (6)	8				

\* Note: Goals that were completed in FY 1999 (met but with no targets beyond FY 1999) were included in this table, but are not reported in this plan.

### Goal/Target Changes Over the Prior Year

The table below provides a general appraisal of the changes in this year’s Annual Report/Plan.

Section	<b>General Appraisal of Changes in the FY 2002 Annual Plan/Report</b> (for specifics, see the detailed goal statements in Part II)																						
<p><b>Research</b> Page 24</p>	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th rowspan="2"></th> <th colspan="4" style="text-align: center;">Fiscal Year</th> </tr> <tr> <th style="text-align: center;">1999</th> <th style="text-align: center;">2000</th> <th style="text-align: center;">2001</th> <th style="text-align: center;">2002</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">Number of Performance Goals</td> <td style="text-align: center;">7</td> <td style="text-align: center;">7</td> <td style="text-align: center;">7</td> <td style="text-align: center;">7</td> </tr> <tr> <td style="text-align: center;">Number of Targets</td> <td style="text-align: center;">12</td> <td style="text-align: center;">12</td> <td style="text-align: center;">15</td> <td style="text-align: center;">15</td> </tr> </tbody> </table> <p><u>Comments</u></p> <ul style="list-style-type: none"> <li>▪ No basic changes in the thrust of the goals in this area.</li> <li>▪ Goal f): Several targets have been added in FY 2001 that mark important new sequencing activities that are underway.</li> </ul>					Fiscal Year				1999	2000	2001	2002	Number of Performance Goals	7	7	7	7	Number of Targets	12	12	15	15
	Fiscal Year																						
	1999	2000	2001	2002																			
Number of Performance Goals	7	7	7	7																			
Number of Targets	12	12	15	15																			
<p><b>Communications</b> Page 141</p>	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th rowspan="2"></th> <th colspan="4" style="text-align: center;">Fiscal Year</th> </tr> <tr> <th style="text-align: center;">1999</th> <th style="text-align: center;">2000</th> <th style="text-align: center;">2001</th> <th style="text-align: center;">2002</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">Number of Performance Goals</td> <td style="text-align: center;">6</td> <td style="text-align: center;">5</td> <td style="text-align: center;">5</td> <td style="text-align: center;">4</td> </tr> <tr> <td style="text-align: center;">Number of Targets</td> <td style="text-align: center;">13</td> <td style="text-align: center;">25</td> <td style="text-align: center;">27</td> <td style="text-align: center;">16</td> </tr> </tbody> </table> <p><u>Comments</u></p> <ul style="list-style-type: none"> <li>▪ FY 2000 – One fewer due to merging two goals into one. FY 2002 – One fewer goal planned as a goal is expected to be completed in FY 2001.</li> <li>▪ Goal a) -- FY 2000 target #5 incorporated a revised plan for the corresponding FY 1999 targets (#1, #2) that were unable to be completed in that year.</li> <li>▪ Goal b) -- NIH’s Assessment Report for FY 1999 erroneously listed FY 1999 target #3 as “not met.” Salud para Su Corazon is presently NIH’s only cardiovascular health outreach program for Latinos. Completing the evaluation of this program in FY 1999 represented full achievement of the intended target in that FY.</li> <li>▪ The FY 2001 targets for goals b), c) and d) were rewritten to provide greater specificity.</li> <li>▪ What has been Goal f) in previous FY plans, concerning activities of the National Library of Medicine (NLM), has been removed, with the targets reassigned under existing Goal c).</li> </ul>					Fiscal Year				1999	2000	2001	2002	Number of Performance Goals	6	5	5	4	Number of Targets	13	25	27	16
	Fiscal Year																						
	1999	2000	2001	2002																			
Number of Performance Goals	6	5	5	4																			
Number of Targets	13	25	27	16																			



Section	<b>General Appraisal of Changes in the FY 2002 Annual Plan/Report</b> (for specifics, see the detailed goal statements in Part II)												
<b>Technology Transfer</b>  Page 188					<table border="1"> <thead> <tr> <th colspan="4">Fiscal Year</th> </tr> <tr> <th>1999</th> <th>2000</th> <th>2001</th> <th>2002</th> </tr> </thead> </table>	Fiscal Year				1999	2000	2001	2002
Fiscal Year													
1999	2000	2001	2002										
Number of Performance Goals	3	3	3	3									
Number of Targets	5	6	7	8									
<p><u>Comments</u></p> <ul style="list-style-type: none"> <li>▪ Goals b and c) – Goal b) is being brought to closure in FY 2000, and being replaced by Goal c), with targets in FY 2001 and 2002. This is being done to provide a better measure of the intended outcomes of this activity area.</li> <li>▪ Goal e) – Expected to be completed in FY 2000, and, thereby, no targets listed after this year.</li> </ul>													
<b>Research Leadership and Administration</b>  Page 208	<i>Priority Setting</i>				<table border="1"> <thead> <tr> <th colspan="4">Fiscal Year</th> </tr> <tr> <th>1999</th> <th>2000</th> <th>2001</th> <th>2002</th> </tr> </thead> </table>	Fiscal Year				1999	2000	2001	2002
Fiscal Year													
1999	2000	2001	2002										
Number of Performance Goals	3	2	1	1									
Number of Targets	6	2	1	1									
<p><u>Comments</u></p> <ul style="list-style-type: none"> <li>▪ FY 2000 – One fewer goal due to goal completion in FY 1999 (goal not carried forward in this plan).</li> <li>▪ FY 2001 – One fewer goal due to goal completion in FY 2000.</li> </ul>													

Section	General Appraisal of Changes in the FY 2002 Annual Plan/Report (for specifics, see the detailed goal statements in Part II)				
<b>Research Leadership and Administration</b>  Page 208	<b><i>Grants Administration and Peer Review</i></b>				Fiscal Year
		1999	2000	2001	2002
	Number of Performance Goals	8	4	5	5
	Number of Targets	8	7	9	6
<u>Comments</u>					
<ul style="list-style-type: none"> <li>▪ 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.</li> <li>▪ Current Goals a), b) c) and d) have been clarified and FY 2000 targets moved from previous goals c), d), f) and g) to better focus on the principle performance elements.</li> <li>▪ FY 2000 targets from previous Goals e) and f) combined under current Goal c).</li> </ul>					
<b><i>Agency Management and Administration</i></b>				Fiscal Year	
		1999	2000	2001	2002
	Number of Performance Goals	11	11	4	2
	Number of Targets	16	13	4	2
<u>Comments</u>					
<ul style="list-style-type: none"> <li>▪ FY 2001 – Seven fewer goals as the goals are being removed after FY 2000 (see below). FY 2002 – Two fewer goals planned as the goals are expected to be completed in FY 2001.</li> <li>▪ Goal b) -- The measures used to track this goal are being revised in FY 2001 and beyond, to better focus on the most relevant measure of performance, which is the dollar volume of orders</li> <li>▪ Goals d-k) – Deemed not to be “mission critical” and are being removed from NIH’s GPRA plan after FY 2000. (Many of these goals/targets are being 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 &amp; administrative matters of only the highest importance in this section.</li> </ul>					

Section	<b>General Appraisal of Changes in the FY 2002 Annual Plan/Report</b> (for specifics, see the detailed goal statements in Part II)				
<b>Training Support and Outreach</b>  Page 284	Fiscal Year				
	1999	2000	2001	2002	
	Number of Performance Goals	5	6	6	6
	Number of Targets	12	10	11	10
<u>Comments</u> <ul style="list-style-type: none"> <li>▪ FY 2000 – One new goal was added in FY 2000.</li> <li>▪ The previously separate (in FY 2001 Annual Plan and earlier) Training Support and Outreach areas have been integrated in the FY 2002 plan. Also, the sequence of presentation of goals has been modified somewhat, to bring the key outcome goals to the front. In some cases, there has been some modest rewording of goal and target statements to clarify the focus of the performance interest</li> <li>▪ Goal a) – This now combines previous year targets that had separately treated application/award rates and related outreach activities have been combined into a single goal.</li> <li>▪ Goal d) -- Used to be part of Goal a) in previous year plans. Due to importance, is separately identified in FY 2002 plan.</li> </ul>					
<b>Intramural Modernization and Improvements</b>  Page 324	Fiscal Year				
	1999	2000	2001	2002	
	Number of Performance Goals	5	5	6	5
	Number of Targets	7	6	9	5
<u>Comments</u> <ul style="list-style-type: none"> <li>▪ FY 2001 – Net increase of one goal. One FY 2000 goal is completed, but two goals are added in FY 2001.</li> <li>▪ Goals c) ,d) e) and f) include notes that provide preliminary budget data. This data is based only on preliminary planning estimates and will be refined in future plans.</li> </ul>					

Section	<b>General Appraisal of Changes in the FY 2002 Annual Plan/Report</b> (for specifics, see the detailed goal statements in Part II)												
<b>Extramural Assistance</b>  Page 352					<table border="1"> <thead> <tr> <th colspan="4" data-bbox="1003 359 1421 405">Fiscal Year</th> </tr> <tr> <th data-bbox="1003 405 1122 449">1999</th> <th data-bbox="1122 405 1219 449">2000</th> <th data-bbox="1219 405 1312 449">2001</th> <th data-bbox="1312 405 1421 449">2002</th> </tr> </thead> </table>	Fiscal Year				1999	2000	2001	2002
Fiscal Year													
1999	2000	2001	2002										
Number of Performance Goals	1	1	1	1									
Number of Targets	1	3	3	3									
<u>Comments</u> <ul style="list-style-type: none"> <li>▪ No basic changes in the thrust of the goals in this area.</li> </ul>													

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## Appendix 3

### Linkage to the 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.

<b>NIH Involvement With DHHS Strategic Goals/Objectives FY 2001-2006 Strategic Plan</b>
<b>Goal 1: Reduce the Major Threats to the Health and Productivity of All Americans</b>
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
<b>Goal 2: Improve the Economic and Social well-being of Individuals, Families and Communities in the United States</b>
Objective 2.3 Improve the healthy development and learning readiness of preschool children
Objective 2.5 Increase the proportion of older Americans who stay active and healthy

<b>NIH Involvement With DHHS Strategic Goals/Objectives                      FY 2001-2006 Strategic Plan</b>
Objective 2.6 Increase independence and quality of life of person with long-term care needs
<b>Goal 3: Improve Access to Health Services and Ensure the Nation’s Health Entitlement and Safety Net Programs</b>
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
<b>Goal 4: Improve the Quality of Health Care and Human Services</b>
Objective 4.1 Enhance the appropriate use of effective health services
Objective 4.3 Improve consumer and patient protection
<b>Goal 5: Improve the Nation’s Public Health Systems</b>
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
<b>Goal 6: Strengthen the Nation’s Health Science Research Enterprise and Enhance Its Productivity</b>
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, 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 depend 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 managers 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

### The NIH's 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 mellitus 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 diseases nervous system in order 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. Including 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 that are 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. It’s 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 some 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.
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

Institute/Center	Mission
	chronic illness and disability, promote healthy behaviors and prevent the onset or worsening of disease, and improve the environment in which healthcare is administered.
National Human Genome Research Institute	NHGRI supports the 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	NCCRR 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	The National Center on 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 the 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	The Clinical Center 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.
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



Institute/Center	Mission
	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.

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