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"Fiscal Year 2001 President's Budget Request for the National Cancer Institute"

Statement of
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Mr. Chairman and Members of the Committee:

I am pleased to appear before you for the fifth time to describe our progress in and hopes for the programs of the National Cancer Institute (NCI).

The Burden of Cancer

Each year, I have begun this testimony by reporting one critical measure of the cancer burden, the annual statistics of cancer incidence, survival rates and mortality. We have recently begun to review the latest numbers and the decrease in overall cancer mortality rates first observed in the early 1990s are accelerating between 1995 and 1997, the latest year for which we have data.

 Figure A - Cancer Death Rates Continue to Fall

Drops continue to be seen for the four major cancer sites of lung, colorectal, breast and prostate. Cancer sites where mortality rates are still increasing include liver and non-Hodgkin's lymphoma. Overall, mortality rate drops are seen in both the black and white population. Remarkably, the magnitude of these drops are such that, for the first time, between 1996 and 1997, the total number of cancer deaths did not rise, despite a growing and aging population.

 Figure B - The Actual Number of People in the U.S. Dying of Cancer Each Year Has Leveled Off

As this Subcommittee has discussed before, the burden of cancer is not equally experienced across our population. Monitoring rates and trends over time, by geography, by gender, age and racial and ethnic groups has been a priority for the NCI. We are particularly concerned about the disproportionate burden of cancer among the poor, the medically underserved and among certain ethnic minorities. In response to our planning processes, we are in the midst of a number of expansions in our programs aimed at the ability to assess, explain and affect the unequal burden of cancer. These expanded and new initiatives address the important message of last year's Institute of Medicine (IOM) report on the unequal burden of cancer.

We are in the process of expanding the Surveillance Epidemiology and End Results (SEER) program (our cancer surveillance program) to enhance coverage of rural whites

and blacks, non-Mexican Hispanics and Native Americans. We are completing a new Memorandum of Understanding (MOU) with the Centers for Disease Control and Prevention (CDC) to formalize collaboration and integration of the NCI's surveillance and surveillance research programs with the CDC's National Program of Cancer Registries. This will allow a strategic integration of the NCI's more intensive surveillance and research system with the CDC-funded state registry systems, to help develop data standards and tools for pooling data.

In FY 2000, we will begin to fund a new research program to create Special Population Networks (SPNs) for cancer control and research. These new consortia will be based within various communities serving different segments of our diverse society in order to establish cancer control and research infrastructures to work within and to serve these communities. To support the activities of these SPNs, we are establishing a cancer control academy at the NCI for training and will link these community-based research networks to the full range of information and communication resources of the NCI. These SPNs, we hope, will provide the basis for a new national platform for cancer research to address the distinct cancer burdens of special populations. We are setting aside $50-60 million over five years to fund about 14 SPNs, the largest program of its kind we have ever funded.

This year, in collaboration with the NIH Office of Research on Minority Health, we began funding five research partnerships between NCI-designated cancer centers and minority institutions to create active and successful research programs linked to our most successful cancer research institutions. We plan to release a new Request for Applications (RFA) to sustain and enhance these new enterprises. A more complete description of our activities in this crucial area can be found at the NCI Office of Special Populations Research Web site.

Monitoring cancer incidence and mortality trends can help us formulate questions about the distribution of cancer control and care, as well as about possible causes of cancer. This year, the NCI released, for the second time in its history, 25-year cancer mortality maps. These cover all 3,100 United States counties and state economic areas, for 40 cancer sites, by gender and race. These maps are available on the NCI Web site in a user-friendly and dynamic format. They do not tell us causes of cancer or indeed whether a geographic pattern reveals either a localized environmental factor, a behavioral pattern or a socio-economic pattern. But, by providing the starting point for addressing these issues, these maps are crucial resources. The NCI will release a Request for Application (RFA) to support two types of studies linked to these maps: epidemiologic research to search for explanations for geographic and temporal cancer patterns, and methodologic research to develop Geographic Information Systems (GIS) for evaluating environmental associations with cancer. These maps are one part of NCI's extensive ($472 million in FY99) program in establishing environmental (exogenous) causes of cancer.

Progress in Basic Research

Progress in our understanding of the biology of cancer continues at an astonishing pace. Let me highlight two examples. For decades, scientists have tried to define the minimum number of molecular changes and the number and nature of molecular pathways that must be perturbed to turn a normal cell into a cancer cell.

 Figure C - Understanding the Molecular Basis of Cancer

This year, NCI-funded investigators identified that alterations of only three genes and four molecular pathways are sufficient to transform a normal human cell to one capable of producing a tumor. These identified pathways are already providing long-sought targets for new therapeutics. Identifying the specific molecular pathways that define each type of human cancer has allowed us to begin to replicate these changes in the genes of mice. As predicted, these mice develop cancer and for the first time, we can accurately mimic human cancer in the mouse. This is allowing us to finally test whether molecular changes associated with human cancer and its development are actually the causes of the progression and behavior of cancer. To accelerate the output of these breakthroughs and to use them to discover and test ways of preventing and curing cancer, we have established the Mouse Models of Human Cancers Consortium, an international collaboration of over 70 institutions. This consortium will support the development and validation of mouse models for human cancer. It is a new research structure that will enable the sharing of reagents and expertise, the development and dissemination of new technologies, the establishment of standards and prioritization of research questions. We hope to expand the activities of the MMHCC to support the development and utilization of these important new cancer research tools.

New Approaches to Detection and Diagnosis

The knowledge that cancer cells develop by changing their molecular profile has set the stage for a new and systematic approach to both early detection and accurate diagnosis. Three years ago, the NCI set out to establish a full index of all the genes that are altered in each type of cancer. This project, called the Cancer Genome Anatomy Project or CGAP, has been extremely successful, identifying tags for the vast majority of human genes, annotating what types of cells and cancers express those genes, developing catalogues of chromosomal changes in cancer and discovering common genetic variations that will help to explain why individuals are different in their risk of getting cancer, their sensitivity to diet and the environment and their response to therapy. CGAP has become one of the most widely used sources of information and reagents in the research world (www.ncbi.nlm.nih.gov/ncicgap/).

As we approach a complete list of all of the molecular tags associated with each cancer and its development, we can systematically search for "markers for the early detection of cancer. To utilize the wealth of discovery coming from CGAP in the development of cancer markers, we have created a new national research infrastructure, called the Early Detection Research Network (EDRN). The EDRN is a novel and complex research structure established to discover, develop and validate markers for the early detection of cancer. Researchers from multiple institutions will work together to assure that potential

markers are prioritized, developed into reliable and standardized assays and validated on readily available and well characterized clinical materials. Four components of the EDRN are now funded: 1) Marker discovery laboratories (18 institutions); 2) Marker development laboratories (2 institutions); 3) Clinical and Epidemiology Centers (8 institutions); and 4) a data and statistical center. In its first year, the EDRN will focus on markers for breast, prostate, ovarian, lung and GI cancers.

Systematic gene discovery through CGAP and other projects is about to profoundly change our approach to the classification and therefore the accurate diagnosis of cancer.

 Figure D - The Importance of Correct Diagnosis

 Figure E - Gene Discovery to Technology

 Figure F - Application to People with Cancer

To do this has required the development and dissemination of new technologies to read the complete molecular profiles of cancer. To enable this, the NCI funded the establishment of 24 "microarray" centers across the country. Next, the institute announced a new funding initiative called the Director's Challenge whose goal is to identify new molecular classification schemes for cancer to replace the purely histologic schemes of the last century. The initial funding established 10 consortia involving 24 institutions addressing breast, prostate, ovarian, colorectal, cancers as well as lymphomas and leukemias. Already, results from these groups are revealing new types and subtypes of cancer that appear to predict which patients will respond to particular therapies. This year, we hope to expand this program to more types of cancer and to define the clinical implications of these new classes of cancers to help predict prognosis and guide the choice of therapy.

Imaging Cancer

Four years ago, the NCI identified imaging as one of its extraordinary opportunities for investment. We have developed new funding mechanisms for exploratory, innovative grants (almost 150 grants received), the establishment of five small animal imaging centers, and the establishment of a national clinical trials network to rapidly evaluate the clinical utility of new imaging approaches. This network, called the American College of Radiology Imaging Network (ACRIN) has a number of clinical trials in preparation including a comparison of Magnetic Resonance (MR) and Computed Tomography (CT) in gynecologic malignancies, the use of Positron Emission Tomography (PET) to follow response to chemotherapy, the value of spiral CT for lung cancer screening, comparative studies of virtual colonoscopy and of digital mammography. We are also funding the development of centers to foster the new field of functional imaging, whereby we can detect not only the presence of a tumor but query its molecular characteristics and its behavior. This year, we will be able to fund 2-3 full multi-disciplinary In Vivo Cell and Molecular Imaging Centers (ICMICs). In addition, 27 institutions have applied to receive planning grants to develop such centers. This year, we created the Unconventional

Innovations Program (UIP) aimed at developing truly novel detection and imaging systems by bringing revolutionary technologies of molecular sensing, nanoscale devices and microexplorers to enable the remote sensing of cancer. We have funded six consortia of investigators to be part of this program and hope to add more members in response to a second release of this Broad Agency Announcement. Over the past year, our investment in imaging research and technology has increased 30%.

Finally this year, the NCI organized a unique forum to bring together academics, industry (through the National Electrical Manufacturer's Association), the Food and Drug Administration (FDA) and Health Care Financing Administration (HCFA) to coordinate practices relevant to the development, testing and adoption of new imaging modalities and applications. This collaborative enterprise will be a standing forum to facilitate communication and progress in this critical area.

Molecular Targets--New Approaches to Prevention & Treatment

For the past three years, the NCI has been redirecting its drug discovery program to one based on the success of basic research in identifying the precise molecular targets implicated in the development (prevention targets) and behavior/survival (therapeutic targets) of cancer.

 Figure G - Cancer Therapy in Evolution

The recent encouraging results of Herceptin for the treatment of advanced breast cancer, Rituximab for the treatment of non-Hodgkin's lymphoma, STI 571 for the treatment of leukemia, tamoxifen for reducing the risk of breast cancer and a growing list of others, all point to the future face of molecularly targeted therapeutics and preventives. We have funded four new centers to develop new libraries of chemical diversity and to screen for promising molecular targets, and this year, we will fund new Centers of Excellence for drug development, each of which will focus on specific cancer pathways to speed the discovery of useful targets.

Last year, we initiated a novel program called RAID (Rapid Access to Intervention Development) that evaluates promising drug candidates in the laboratories of academic investigators and, via peer review, manages the movement of these candidate drugs from the lab to the point of clinical trial. To date, 32 novel agents have entered the RAID pipeline and in one year 4 have reached or are ready for clinical trials. We will expand this successful program in the coming year.

Clinical Trials--A Cornerstone of Progress for Patients

Last year, the NCI supported over 1500 clinical trials in prevention and treatment, covering virtually all human cancers and asking a wide variety of clinical questions. We initiated the formal restructuring of our national clinical trials system, as described to the Subcommittee last year. This restructuring is aimed at improving the quality of scientific questions asked, increasing the speed and efficiency and decreasing the administrative

burdens of participating in clinical trials. Furthermore, it aims to assure that all patients and all participating physicians have access to the full menu of available clinical trials. This year, we continued the development and deployment of a standard informatics system, funded a central Clinical Trials Support Unit to serve the entire national clinical trials system and began disease-specific state-of-the-science meetings to develop prioritized clinical trials questions and opportunities. This past year, 20,000 new patients were enrolled in NCI-sponsored treatment trials. Over the past three fiscal years, our investment in our national clinical trials program has increased almost 43%.

Clinical trials are complicated enterprises, and streamlining and improving their function while maintaining the highest standards of rigor, care and protection of human subjects requires attention to many different facets of the initiation, review, approval, funding, oversight and management of trials. This year, we have continued to expand the use of simplified and uniform informed consent documents and in the spring, in collaboration with the Office for Protection from Research Risks (OPRR), we will begin an important pilot project to test the feasibility and performance of a central Institutional Review Board (IRB) for multi-institutional trials.

This year, we unveiled a new, user-friendly clinical trials information system to enable patients and physicians to readily access information about all NCI-sponsored trials (cancernet.nci.nih.gov). We continue to work with the FDA and industry to expand this database to include industry and other sponsored trials.

Each year, clinical trials results help shape the course of clinical practice and set the stage for new questions that need to be addressed. This year, we saw the first, long-awaited results on the value of high dose chemotherapy with peripheral stem cell or bone marrow rescue for women with advanced breast cancer. These results did not support the significant and hoped-for benefits that this approach demonstrated in earlier, non-randomized clinical trials. These results underscored the crucial role that such clinical trials play in the type of evidence-based medicine to which we all aspire. In the past two years, the results of clinical trials have set new standards for increasing the effectiveness and reducing the toxicity of regimens for childhood cancers, leukemia, myeloma, breast cancer, ductal carcinoma in situ (DCIS), cervical cancer, head and neck cancer, lymphoma, colorectal cancer, prostate cancer and others.

Quality Cancer Care--A Research Agenda

One of the themes of NCI activities is to address gaps--gaps between what we need to know and our current state of knowledge, gaps between the burden of cancer across different segments of our population, and gaps between scientific discovery and medical breakthroughs. One of the most important gaps is between evidence-based best practice and actual practice. It is this last gap that we intend to address via a new major initiative called the Quality Cancer Care Committee (QCCC). This initiative was formulated in response to a recent report of the National Cancer Policy Board (NCPB) called "Ensuring Quality Cancer Care." The NCPB was established at my request as part of the Institute of Medicine (IOM) of the National Academy of Sciences. Its purpose is to provide a forum

of independent and broad-based expertise to advise the Nation on cancer-related policy issues. The QCCC will be a trans-agency initiative led by the NCI to develop a comprehensive research infrastructure to address the issues of quality cancer care across the cancer continuum from prevention to treatment to survivorship and end-of-life care; and to provide a mechanism whereby the health delivery and reimbursement activities of DHHS, especially HCFA, are informed by a discussion of evidence and through direct interaction with the cancer research agenda of the various research agencies of the Department. The research agenda of the QCCC will focus in four areas: 1) developing measures of cancer outcomes; 2) strengthening the methodologic and empiric base for quality assessment; 3) strengthening the national clinical trials infrastructure; and 4) improving the quality of cancer communications.

I am pleased to present the President's non-AIDS budget request for NCI for FY 2001, a sum of $3.25 billion which reflects an increase of $183 million over the comparable Fiscal Year 2000 appropriation. Including the estimated allocation for AIDS, total support requested for NCI is $3.505 billion an increase of $193 million over the Fiscal Year 2000 appropriation. Funds for the NCI efforts in AIDS research are included within the Office of AIDS Research budget request. With this, we can sustain the many new and productive programs, some of which I have tried to illustrate in this testimony.

NIH budget request includes the performance information required by the Government Performance and Results Act (GPRA) of 1993. Prominent in the performance data is NIH's first performance report which compares our FY 1999 results to the goals in our FY 1999 performance plan. As our performance measures mature and performance trends emerge, the GPRA data will serve as indicators to support the identification of strategies and objectives to continuously improve programs across the NIH and the Department.