DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NATIONAL CANCER INSTITUTE

Fiscal Year 2007 Budget Request

Witness appearing before the
House Subcommittee on Labor-HHS-Education Appropriations

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BUDGET STATEMENT

The fiscal year FY 2007 budget includes $4,753,609,000, a decrease of $39,747,000 below the FY 2006 enacted level of $4,793,356,000 comparable for transfers proposed in the President's request.

OUR GOAL REMAINS THE SAME

Four years ago, we put the NCI on a trajectory towards the Challenge Goal of eliminating suffering and death due to cancer as early as the year 2015. Since that time, we have vigorously and aggressively managed NCI's portfolio of investments in cancer research across that entire continuum of the process of cancer, whether we've been focusing on understanding genetic mutations that were responsible for susceptibility to cancer or focusing on issues that have to do with survivorship and living with, rather than dying from, cancer.

NCI has been a major leader in the molecular metamorphosis of biomedical medicine that has benefited all fields of medical research. Without the Nation's support of NCI's pioneering role in funding research – including basic science, clinical trials, and translational investigations – into the molecular and genetic processes that underlie all disease and the training of new cancer researchers, it is unlikely that the advances we are seeing today in many health areas – from AIDS to macular degeneration – would have occurred at the pace they have. These leadership efforts must be sustained going forward.

The Nation's past commitment to cancer research has proven its worth: mortality rates have declined for all cancers combined while incidence rates have stabilized or increased slightly, detection and treatments have improved, new

therapeutic options offer startling promise. Today there are nearly 10 million cancer survivors in the United States compared to approximately 3 million cancer survivors in 1971 when the National Cancer Act was established. Also, in 1971 fewer than half of those found to have cancer lived 5 years beyond their diagnosis; today the 5 year survival rate is 64% for adults and 79% for children aged 14 or younger. The latter figure is truly remarkable given how few children survived even a couple of years after being diagnosed in the early 1970s. NCI's continued commitment is manifested today in far-reaching programs that have advanced our basic understanding of the genetic changes responsible for this dreaded disease. The Nation's investment and the actions of Congress are directly responsible for the development of a nation-wide network of 61 NCI-designated cancer centers and a highly successful Community Clinical Oncology Program (CCOP), founded in 1983. Through the network of 64 CCOP grantees, community investigators participate actively in NCI-sponsored cancer prevention, control, and treatment clinical trials. These programs place cutting-edge research directly in communities and put access to cancer clinical trials into the hands of local physicians. Because of their participation in NCI trials, community clinicians more readily adopt new regimens, ensuring that these advances are rapidly made part of the standard of care.

Recently, NCI's leadership team has initiated a series of site visits to innovative community-based cancer centers as potential models for a new NCI initiative, the Community Cancer Centers Program (CCCP). The CCCP would help foster replication of successful community models across the country, set the standards for multi-specialty state-of-the-art care, provide access to early phase clinical trials, and

ultimately improve cancer care and outcomes. This program is especially designed to bring academic standards of care and clinical trials directly to the segments of our population who either through age or resources cannot leave their community.

A RECORD OF REAL SUCCESS

The past year in cancer research shows a record of substantial and heartening achievement. We are expanding our foundation of knowledge and the technical tools with which rapid advances can be made in understanding the mechanisms of cancer. We are exponentially increasing the opportunities to manage this lethal disease. Building on NCI-funded research, large-scale clinical trials in 2005 yielded results that will have profound effects in preventing and treating many cancers.

For example, three different clinical trials showed that adding trastuzumab (Herceptin ®) to standard adjuvant chemotherapy significantly reduced the risk of recurrence in women with the early-stage breast cancer, HER-2/neu positive, which has an over expression of protein in the gene. Approximately 50,000 women in the United States are diagnosed with HER-2/neu positive breast cancer each year, representing about 20% of invasive breast cancers.

Equally stunning results were seen in the trial of a vaccine that protects against two strains of human papillomavirus (HPV) that cause over 70% of cervical cancers, a disease that kills more than 200,000 women each year, including many in developing countries. Study results concluded that women who received the vaccine during a 2-year study were protected against precancerous lesions caused by HPV. NCI made the initial discoveries linking HPV to cervical cancer, which led to creation and testing of HPV vaccines that are based on technology also developed at the Institute. It is an

outstanding exemplar in this era of molecular medicine of how NCI's knowledge about the etiology of the disease enabled creation of a vaccine against a specific cancer.

In January, an NCI-sponsored trial reported that women who received chemotherapy directly in their abdomens as part of treatment for advanced ovarian cancer lived more than a year longer than women who received the same chemotherapy intravenously. The findings confirm and expand recent research showing that intraperitoneal (IP) chemotherapy, which delivers drugs directly to the abdominal cavity through a catheter, can significantly increase survival for some women with the disease. As the results were made public, NCI issued a rare clinical announcement to raise awareness about IP chemotherapy for ovarian cancer among physicians and patients. The NCI announcement - the first since 1999 - was warranted because IP chemotherapy is widely regarded as an old technology and previous trials have generated little interest among physicians. Ovarian cancer causes the most deaths of any gynecological cancer in the United States and frequently goes undetected until tumors spread beyond the ovaries.

Another notable advance came last September with the announcement of results from the NCI-sponsored Digital Mammographic Imaging Screening Trial (DMIST). The study found that digital mammography is more accurate than film mammography for women with dense breasts, as well as for several other groups of women, including women under 50 and pre- and perimenopausal women. Overall, DMIST offers a model case study of how NCI can be an agent of change, pursuing new approaches to research, partnering with the private and public sectors, and fueling the development of technologies to achieve an important advance. It is particularly noteworthy that NCI

and the American College of Radiology Imaging Network (ACRIN) secured the involvement in DMIST of four companies that developed and manufactured digital mammography machines for our use in clinical trials: Fischer Medical, Fuji Medical, General Electric Medical Systems, and Hologic.

Finally, NCI has made strides to address the widespread disparities in cancer screening, treatment, and care for disadvantaged, mostly minority populations. One approach to closing this access gap is NCI's Patient Navigator Research Program, which relies on personal guides to shepherd disadvantaged cancer patients into standard care. NCI supports a number of Patient Navigator Program pilot projects in minority communities and about $24 million in grants will be awarded over the next 5 years as part of the program.

ADVANCED TECHNOLOGIES ACCELERATE PROGRESS

The technology revolution is speeding up and enabling the discovery process. Nanotechnology has emerged as a key strategy for imaging molecular features of cancer and will ultimately lead to personalized medicine. NCI's investment in nanotechnology is a powerful example of leveraging resources from the private sector through our Centers of Cancer Nanotechnology Excellence.

Of equal significance, in December 2005 NCI and the National Human Genome Research Institute (NHGRI) launched The Cancer Genome Atlas (TCGA) Pilot Project, a comprehensive effort to accelerate understanding of the molecular basis of cancer and which evolved from the Human Genome Project (HGP). The TCGA Pilot Project will develop and test the science and technology needed to systematically identify the genetic changes in a small number of cancers.

Additionally, NCI's cancer Biomedical Informatics Grid (caBIG™) is creating a unifying technology platform or "world-wide web" for cancer research. caBIG™ is well on the way to its goal to create a network of interconnected data, applications, individuals, and institutions that will redefine how cancer research is conducted and care is provided. This initiative has also whetted considerable commercial interest.

INTERAGENCY COLLABORATIONS

Addressing the cancer problem requires that NCI work across institutional and sector boundaries, share knowledge, and bring together the diverse members of the Department of Health and Human Services (DHHS) family of agencies, as well as other federal offices, that can help develop systems-based solutions to the cancer problem.

The NCI and FDA Interagency Oncology Task Force (IOTF) continues to remove bottlenecks in the process of developing and approving safe, more effective cancer interventions. During 2005, IOTF helped foster the creation of two important initiatives: the Exploratory Investigational New Drug (IND) process to streamline the early clinical development of new drugs and biologics; and the NCI Regulatory Affairs Liaison position to help NCI-funded researchers navigate through FDA's IND application process. Both will help eliminate obstacles to the rapid development of promising new anticancer agents.

DHHS Secretary Mike Leavitt announced last month the Oncology Biomarker Qualification Initiative (OBQI) – an unprecedented interagency agreement among NCI, FDA, and the Centers for Medicare and Medicaid Services (CMS) to collaborate on improving the development of cancer therapies and the outcomes for cancer patients through biomarker development and evaluation.

CONCLUSION

We must do more to continue the acceleration of discovery, development, and delivery of the interventions that will hasten the transformation of our traditional view of cancer as a death sentence into a disease that we can prevent, eliminate, or control. This will be the legacy we leave our children.

While progress is evident, there is much that remains to be accomplished. We are committed to face the challenge of making difficult choices between those programs that we will continue to grow and nurture and those that have already advanced our knowledge. The decisions will be science driven. This is an unprecedented era of discovery. The opportunities to apply powerful new technologies to advance our knowledge and the opportunities to change the course of cancer have never been greater.

John E. Niederhuber, M.D.
Biographical Sketch

John E. Niederhuber, M.D., is Deputy Director, National Cancer Institute (NCI) and Deputy Director for Translational and Clinical Sciences, NCI, National Institutes of Health. He assumed this position in October 2005. He was formerly the Wattawa Professor-Bascom in Cancer Research, Professor of Surgery and Oncology at the University of Wisconsin School of Medicine. Dr. Niederhuber served the University of Wisconsin as the Director of the University of Wisconsin Comprehensive Cancer Center from July 1997 until October 2002. He came to the University of Wisconsin in 1997 from Stanford University where he had served as Chair of the Department of Surgery. In June 2002, President George W. Bush appointed Dr. Niederhuber Chair of the National Cancer Advisory Board, a position he held until resigning to become the Deputy Director at NCI.

Dr. Niederhuber is a nationally recognized cancer surgeon with a special clinical emphasis in gastrointestinal cancer, hepatobiliary cancer and breast cancer. He is recognized for his pioneering work in hepatic artery infusion chemotherapy and was the first to demonstrate the feasibility of totally implantable vascular access devices. Dr. Niederhuber has been a member of the Society of Surgical Oncology since 1978 and served as SSO President (2001-02). He also served as President of the American Association of Cancer Institutes (AACI) (2001-03). Dr. Niederhuber was one of the founding members and served on the executive committee of the American College of Surgeons Oncology Cooperative Group.

His laboratory research interests focus on protein tyrosine kinases and signal transduction in normal and abnormal cell growth. Trained as an immunologist, Dr. Niederhuber's laboratory worked for many years studying the role of the murine major histocompatibility complex immuoregulatory genes. In recent years, his laboratory has had a specific interest in the regulation of the expression of tyrosine kinases, especially *blk*, a B-cell specific kinase, both at the transcriptional and translational level. The *Blk*-proto-oncogene was a novel discovery in Dr. Niederhuber's laboratory while he was a member of the faculty at The Johns Hopkins Medical School and is of interest because of its unique expression in B-cells and its participation in both proliferative and apoptotic pathways during B-cell differentiation. His laboratory has demonstrated the presence of an *Internal Ribosomal Entry Site* (IRES) within the 5' UTR of *blk* mRNA. This discovery has raised the possibility that *blk* function may depend on whether translation occurs in a cap-dependent or cap-independent IRES mediated manner. The laboratory is also interested in a class of genes expressing proteins described as KH-binding domain proteins. This class of proteins has RNA-binding capacity and act to prolong mRNA stability for translation.

Dr Niederhuber has considerable experience as a leader in the cancer field. He served as a member of the NCI Cancer Center's Review Committee (1984-86) and the NCI Division of Cancer Treatment Board of Scientific Counselors (1986-1991). He was Chairman of the Board from 1987-1991. He was a member of the NCAB Subcommittee to Evaluate the National Cancer Program (Committee to Assess Measures of Progress Against Cancer), chairing the Molecular Medicine Panel (1993-95). He was a member of the American College of Surgeons Commission on Cancer

from 1983-95, chairing the commission from (1989-90). Dr. Niederhuber has served on the General Motors Cancer Research Foundation Kettering Prize Selection Committee (1988-89) and twice served on the GMCRF Awards Assembly (1988-92), (1998-02). Dr. Niederhuber served on ASCO's Public Issues Committee from 1985-86 and the Nominating Committee in 1993. Dr. Niederhuber chaired the ASCO Surgical Oncology Task Force for the 2001-02 strategic planning process. He chaired the ASCO Public Policy and Practice Committee (2002-2003). He is a member of the Burroughs-Wellcome Foundation Translational Research Advisory Committee (1999-06).

Dr. Niederhuber is a graduate of Bethany College, Bethany, West Virginia and the Ohio State University School of Medicine. He was an NIH Academic Trainee in Surgery at the University of Michigan (1969-70) and a Visiting Fellow, Division of Immunology, The Karolinska Institute, Stockholm, Sweden (1970-71). He completed his training in surgery at the University of Michigan in 1973. He was a member of the faculty of the University of Michigan from 1973 to 1987, being promoted to Professor of Microbiology/Immunology and Professor of Surgery in 1980. During 1986-87, he was Visiting Professor in the Department of Molecular Biology and Genetics, The Johns Hopkins University School of Medicine.

Dr. Niederhuber joined the faculty at The Johns Hopkins School of Medicine in 1987 as Professor of Surgery, Oncology, and Molecular Biology and Genetics. In 1991, He was appointed Emile Holman Professor of Surgery, Professor of Microbiology and Immunology and Chair of the Department of Surgery, Stanford University. He left Stanford in 1997 to become the Director of the University of Wisconsin Comprehensive Cancer Center where he guided the consolidation of the University's two distinguished NCI supported cancer centers.

Dr. Niederhuber was recipient of a U.S. Public Health Service Career Development Award from NIAID (1974-79). In 1978 he received the Distinguished Faculty Service Award from the University of Michigan. He has also been recognized with the Alumni Achievement Award from The Ohio State University College of Medicine in 1989 and the Distinguished Alumni Award in Medicine from Bethany College (1995). He was elected to *Who's Who in America* in 1998 and *Who's Who in Medicine and Health Care* (1997). In addition, he has received numerous honorary professorships and is currently serving on the editorial board of ten scientific journals. He was a member of the editorial board of the *Journal of Clinical Oncology* (1993-95). He has authored and coauthored more than 180 publications and edited four books, including, with distinguished colleagues, the highly regarded reference text *Clinical Oncology* which is currently in its third edition.

He has served as an advisor to a number of cancer centers, a number of cancer foundation boards and NCI committees. Dr. Niederhuber is a member of the Board of C-Change, formerly the National Dialogue on Cancer, led by President George H.W. Bush, Mrs. Barbara Bush and Senator Dianne Feinstein. Dr. Niederhuber has also served the as co-chair of the CEO Roundtable task force to develop a plan for future oncology drug development and was recently appointed by former President Bush as a member of the prestigious CEO Roundtable.

Department of Health and Human Services
Office of Budget
Richard J. Turman

Mr. Turman is the Deputy Assistant Secretary for Budget, HHS. He joined federal service as a Presidential Management Intern in 1987 at the Office of Management and Budget, where he worked as a Budget Examiner and later as a Branch Chief. He has worked as a Legislative Assistant in the Senate, as the Director of Federal Relations for an association of research universities, and as the Associate Director for Budget of the National Institutes of Health. He received a Bachelor's Degree from the University of California, Santa Cruz, and a Masters in Public Policy from the University of California, Berkeley