DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2007 Budget Request

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

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Mr. Chairman and distinguished members of the subcommittee, it is an honor and a privilege to appear before you today to present the National Institutes of Health (NIH) budget request for Fiscal Year 2007 and discuss the priorities of NIH for this year and beyond.

Budget Request

The request for NIH is $28.4 billion in FY 2007, the same as the FY 2006 level for the Agency. The budget request will support the research programs managed by NIH's Institutes and Centers. At this budget level, NIH will increase the biodefense research program by $110 million for Advanced Development. Support for the Pandemic Influenza Preparedness Plan will increase by $17 million. We have also chosen to carefully invest in several trans-NIH strategic initiatives. The NIH Roadmap, an incubator for new ideas and initiatives that will accelerate the pace of discovery, increases by $113 million. We allocated $40 million to the Institutes and Centers to launch the Genes, Environment and Health Initiative to accelerate discovery of the major genetic and environmental factors for diseases that have a substantial public health impact. We have also directed $15 million to the new "Pathway to Independence" program to increase our support of new investigators.

I will focus my testimony on the return of the investment in NIH for the American people. In particular, I will discuss how discoveries fueled by this investment are transforming the practice of medicine. We can now clearly envision an era when the treatment paradigm of medicine will increasingly become more ***predictive, personalized and preemptive***. We will strike disease before it strikes us with the hope of greatly reducing overall costs to society. We expect to move away from the costly and predominantly curative model of today, which requires us to wait for the disease to occur before intervening. I will share with you the strategic vision of NIH and discuss the many management innovations we have implemented to ensure optimal stewardship of taxpayers' resources.

Selected Accomplishments of NIH and their Impact on Health

The achievements of NIH and our private sector partners in medical research are difficult to overstate. According to the latest report on the Nation's health from the Centers for Disease Control and Prevention (CDC), life expectancy continues to rise, now at an unprecedented 78 years for the total U.S. population. Since 1950, the age-adjusted death rate for the total population declined by a remarkable 43 percent. Life expectancy has increased by one year in every five for the past 30 years. Americans are not only living longer, they are healthier. For instance, the disability rate of American seniors dropped by almost 30 percent in the past 20 years, owing to a range of scientific advances.

The following are samples of the many advances driven by the investment in NIH.

Advances in Cardiovascular Disease and Stroke

Thirty years ago, it was common for a man or woman to suddenly die of a heart attack or stroke between the ages of 50 and 60. Had this trend continued unabated, today more than 1.6 million lives would have been lost per year. Fortunately, today the toll is much less. The death rates from cardiovascular disease have declined by 63 percent and by 70 percent for stroke. Were it not for the ground-breaking research on the causes and treatment of heart disease, supported in large part by NIH, including recent developments such as drug coated stents, safe levels of blood pressure and cholesterol lowering therapies, heart attacks would still account for 1.2 to 1.3 million deaths per year instead of the actual 515, 000 deaths experienced today. The estimated total cumulative investment in cardiovascular research at the NIH per American over the past 30 years, including the doubling period, is about **$**110, or about **$4 for each American per year** over the entire period.

Advances in Cancer

The mortality rates of cancer, the second leading cause of death in the United States, have been falling for several years, and this year, for the first time in history, the absolute number of cancer deaths in the United States has decreased. More effective therapies have led to improved outcomes for more than 10 million American cancer survivors. With the increase in budgets between 1999 and 2003, the National Cancer Institute has stimulated a paradigm shift in cancer therapy. We are seeing the emergence of targeted therapies, with the unprecedented ability to use specific molecular targeting to treat tumors with novel agents. We can also detect and treat cancer at earlier stages. The National Cancer Institute's (NCI) Early Detection Research Network (EDRN), launched in 1999, has identified a number of biomarkers that allow for the earlier detection of breast, prostate, colon, lung and other cancers. This year, NCI, in collaboration with the Human Genome Research Institute, has launched a cancer genome pilot project to help further our understanding of the basic biology of cancer and identify additional treatment targets. The estimated total cumulative investment at the NCI per American over the past 30 years, including the doubling period, is about $258, or about **$9 per American per year** over the entire period.

Advances in HIV/AIDS

Without the development and testing of antiretroviral drugs, there would be no hope for patients with HIV/AIDS. The development of Highly Active Antiretroviral Therapies primarily resulted from the work of a large cadre of NIH-supported scientists and their counterparts in the pharmaceutical industry. Their discoveries about the cellular mechanisms of the disease have transformed AIDS into a manageable disease, preventing hundreds of thousands of hospitalizations and early deaths. To date, 21 antiretroviral drugs and 4 combination formulations have been approved by the FDA. Many more less toxic AIDS drugs are currently in development. Today, fewer than 50 HIV-infected babies are born each year in the United States, sparing 16,000 to 20,000 children from AIDS through the use of antiretroviral drugs to prevent mother-to-child transmission.

Mother-to-child transmission rates in developing countries have declined by 40 percent with the use of drug therapy. With the introduction of these new drugs, economists estimate the aggregate potential value of improved survival has been nearly $400 billion for those infected through 2000. They estimate the aggregate potential value for all past and future cohorts of individuals infected with HIV is almost $1.4 trillion.

With the additional resources provided during the doubling of the NIH budget, we launched the Vaccine Production Program (VPP) Laboratory to efficiently translate candidate research vaccines, including HIV vaccines, into useable products. Since its inception in 2001, this program has overseen the manufacture of over 29 bulk pharmaceutical compounds formulated into 14 different vaccine products for HIV, as well as West Nile, SARS and Ebola Virus, and expanded our network of clinical trial sites across the globe. This program is enabling NIH to serve the needs of the American people in an age of global risks of infectious diseases.

Advances Against the Threat of Pandemic Influenza

Thanks to fundamental advances in viral genomics and genetic engineering, NIH has been able to help in the development of countermeasures against both seasonal and pandemic influenza viruses. We now have a vaccine against the H5N1 virus and will develop a second one in conjunction with CDC. Without such a vaccine, and others under development and testing, we would be completely defenseless against the potential pandemic that threatens the entire world. We are investing in research and development to hasten the production process by converting from egg-based to cell culture-based vaccines. We are developing novel vaccine approaches using a variety of molecular biological techniques, and we launched discovery efforts for new anti-viral compounds against pandemic flu. We initiated a project to identify the genomes of thousands of human and avian influenza viruses, and, to date, 831 influenza genome sequences from human isolates have been deposited in NIH's GenBank, allowing researchers across the world to better understand influenza viruses and develop countermeasures.

Development of Biodefense Research

Sine 2001, NIH has directed more than $10 billion toward protecting the American public from bioterrorism. The 2001 intentional release of anthrax underscored the reality of a bioterrorism threat posed by other Category A agents such as smallpox, plague, tularemia, hemorrhagic fevers, and botulinum toxin. NIH responded swiftly. Promising vaccine candidates for Ebola and smallpox are currently in clinical trials. Identification of the three-dimensional structure of the anthrax toxin complex is fueling the search for compounds that block the toxin's effects, and the discovery of the key mechanism of Ebola virus cell entry prompted experiments demonstrating that Ebola infection could be blocked in laboratory tests. We continue to build a national biodefense research infrastructure that will position the Nation to respond even more quickly and precisely to bioterrorism.

Advances in Diabetes and Related Illnesses

Nearly 21 million Americans have diabetes, a disease that can cause damage to multiple organs and lead to death. Without NIH research, the improvements of the past two decades in the therapies for diabetes would not have occurred. Through large prospective trials, made possible by the doubling of our budget, we have assessed the relative value of drug based approaches versus weight loss and physical activity, and showed it is possible to reduce the risk of type 2 diabetes by 58 percent with lifestyle modifications alone.

Diabetes can also result in vision loss. Four million American adults suffer from diabetic retinopathy, the outcome of damage to the tiny blood vessels in the light-sensitive retina lining the inside of the eye. Nearly a million have the advanced vision-threatening stage of the disease. The National Eye Institute completed a series of landmark clinical trials to develop novel treatments for diabetic retinopathy. Without these new treatments, 450,000 patients who have advanced disease today would otherwise likely be blind in 5 years. As a consequence, of those currently at risk, only 27,000 would progress to legal blindness, and only 9,000 would become blind today. In addition to reduced suffering and disability, the economic savings from these treatments will reach as much as $1.6 billion per year.

As another example of payoff from recent NIH research, end-stage renal disease (ESRD)-kidney failure requiring dialysis or transplantation, a complication of diabetes and high blood pressure- results in direct federal expenditures of approximately $20 billion per year. Through the 1980s and 1990s, the incidence of ESRD nearly doubled each decade, but in the last five years overall rates have stabilized—and even declined in certain population groups. This improvement has been driven by monitoring for proteins in urine to prevent kidney disease or detect it in its early stages. Compared with earlier projections, the savings in federal health care expenditures are approximately $1 billion dollars per year.

Without the investment in medical research, people with diabetes would be living shorter, less productive, and less hopeful lives.

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Advances in Image-Guided Microsurgery

Increases in the NIH budget allowed new investments in the use of imaging technologies like CAT scanning, MRI or ultrasonography for the development of new microsurgical techniques. These minimally invasive therapies are changing the fate of many patients, including patients with Parkinson's disease, through deep brain stimulation. These new techniques are also promising to revolutionize the treatment of epilepsy, a disease that affects over 2.7 million Americans. As we move forward with such research, we expect that surgery will become less invasive, more precise and less dangerous, with far less operative complications.

Advances in Health Information for Scientists and the Public

The National Library of Medicine of the NIH provides the American public with high quality, reliable information. The NIH web sites (www.nih.gov) are now recognized by independent organizations as the most successful health related web sites, with over 2 million queries per day. Millions of patients and their families regularly consult NIH web sites for up to date information in English and Spanish, a capability made entirely possible by the doubling of the NIH budget. The web-based ClinicalTrials.gov represents a landmark effort to provide information to patients and physicians across the country on NIH-funded clinical trials.

NIH also leads the research field in developing information technology for biomedical research. No biomedical scientist develops a project without first consulting the suite of powerful informational research tools available through the NIH National Library of Medicine's PubMed, a growing digital archive of peer-reviewed research articles and scientific databases.

New Research Tools

NIH researchers have pioneered powerful new research tools and methods such as high throughput DNA sequencing, protein identification with mass spectrometry, gene expression arrays, the determination of thousands of new protein structures, and imaging technologies which were simply unavailable before the doubling of the NIH budget. A great illustration of the impact of these advances has been the identification of the cause of the SARS virus in less than a month and the current tracking of pandemic flu viruses. These tools have greatly accelerated the research process itself, spurred progress and spawned new discoveries in all areas of biomedical research. Perhaps nowhere else have these technological advances in imaging and genotyping elicited more excitement than in the field of mental and behavioral health, elucidating genes linked to schizophrenia, depression, bipolar disorder and anxiety. These discoveries are allowing for the first time direct visualization of brain structure and function to study the brain circuitry involved in thinking and a range of behaviors.

New Diagnostic and Therapeutic Technologies

Some of NIH's successes can be measured in new medical technologies. Advances in research are driving an increase in the number of technologies being licensed to companies for commercialization. In FY 2004, there were thousands of active licenses between federally funded research institutions and companies worldwide. Out of these technologies, several thousand companies are making many new products that have an immeasurable impact on public health. Today, from NIH funded research, more than 300 new drug products and vaccines targeting more than 200 diseases — including various cancers, Alzheimer's disease, heart disease, diabetes, multiple sclerosis, AIDS and arthritis — are in clinical trials. These outcomes are accomplished through the on-going network of successful collaborations with our colleagues in private industry.

The Changing Landscape of Disease

Disease and injury are constant threats to humankind and are never static. New diseases can emerge at any time, such as HIV/AIDS, SARS, Pandemic Flu, obesity or many other conditions. Bioterrorism did not figure significantly in the NIH agenda in 2001, but is now a top priority of the agency. Twenty years ago the impact of Alzheimer's disease was not fully appreciated, nor were its causes known.

As the result of our success in preventing and treating acute and short term conditions such as heart attacks, stroke, cancer and many infectious diseases, we are living longer. Our increasingly older population faces the new challenge of multiple chronic conditions which now consume about 75 percent of healthcare expenditures. This shifting burden of health care from acute to chronic diseases is perhaps the greatest challenge we face.

Health care costs in the United States have risen to more than $2 trillion. The amount spent on health care per person has doubled, from $3,461 in 1993 to $7,110 today. The causes of health care inflation are varied and complex, requiring different, nation-wide solutions.

We are in a race against the overwhelming human and economic consequences of disease. We can win this race, but only if we use research discoveries to transform medicine as we know it. Thanks to recent research advances, we can foresee a future of more effective medical treatment that might be less expensive than current practices.

Strategic Vision for NIH: from Curative to Preemptive Care

We are in an era of great scientific opportunity. Advances in our understanding of basic human biology allowed NIH to sequence the human genome by 2003, two years ahead of schedule, and to complete the Haplotype Map, showing the variation between individual humans, in October 2005, also ahead of plans. One of the greatest scientific achievements in history, the genome blueprint, along with work in systems biology and proteomics, are driving a revolutionary period in the life sciences. We are on the brink of transforming medical treatment in the 21st Century. Our hope is to usher in an era where medicine will be ***predictive, personalized and preemptive.***

Toward this goal, NIH is strategically investing in research to further our understanding of the fundamental causes of diseases at their earliest molecular stages so that we can reliably ***predict*** how and when a disease will develop and in whom. Because we now know that individuals respond differently to environmental changes according to their genetic endowment and their own behavioral responses, we can envision the ability to precisely target treatment on a ***personalized*** basis. Ultimately, this individualized approach, completely different than how we treat patients today, will allow us to ***preempt*** disease before it occurs.

Consider, for instance, how better predictive and personalized treatments could improve the safety and effectiveness of drugs. As we know, drugs do not fall into the "one size fits

all" category. The same drug can help one patient and harm another. Recent research shows that we will be increasingly able to know which patients will benefit from treatment and which patients might be harmed. This field of study is known as pharmacogenetics. Using the latest genomic data, enabled by the doubling of the NIH budget, the NIH established a Pharmacogenetic Research Network which is studying the interactions of drugs and molecules as well as the biological processes that eliminate compounds from the body. In the first five years of this program, the researchers in this network made numerous discoveries.

For example, they learned that 10 percent of the North American population exhibits a genetic variation that puts them at high risk for life-threatening reactions to irinotecan, a cancer drug. We now know that patients with this variation should be given lower than prescribed doses of this successful drug, thus potentially saving their lives.

NIH researchers also discovered variations in a gene involved in the body's response to more than half of all medications. Understanding these differences could explain critical individual as well as racial and ethnic differences in drug responses. Other genetic variations discovered by the NIH network will have an impact on asthma treatment, the risk of sudden death from irregular heartbeats and the proper use of blood thinning medications to avoid deadly bleeding complications.

In another example of emerging personalized medicine, cancer researchers have developed a test that helps determine the risk of recurrence for women who were treated for early stage, estrogen-dependent breast cancer. This information can help a woman and her doctor decide whether she should receive chemotherapy in addition to standard hormonal therapy. This test has the potential to change medical practice by sparing tens of thousands of women each year the unnecessary and harmful side effects associated with chemotherapy at large potential cost savings.

Rapid Advances in the Genomic Era

Because of a hundred fold reduction in the cost of genomic technology, we can now study, at affordable costs, the differences between patients who have a disease and their normal counterparts. Recently, this revolutionary approach led to the discovery of two previously unsuspected factors that can identify who is at risk and how to protect patients from age-related macular degeneration, an increasing cause of blindness in our aging population, with over 7 million Americans at risk. Last month, a key transcription factor that may be responsible for a large percentage of cases of diabetes was discovered.

These breakthroughs form the basis of our budget request for the Genes and Environment Initiative, supported by Secretary of Health and Human Services Michael Leavitt, because it will give us the unprecedented ability to discover, over the next three years, the potential causes of the 10 most common diseases afflicting the U.S. population. With this funding, if approved, we will also launch a technology development effort for enabling scientists to measure many types of environmental exposures at the individual level.

Taken together, these efforts will lead to better understanding of the environmental and genetic factors in the development of many diseases.

Imagine a world where we will be able to tell each patient whether they need to take action to preempt altogether the development of costly and painful diseases. Imagine telling them that they do not need to take expensive medications for life because they are not at risk of disease. A more ***predictive, personalized and preemptive*** form of medicine is no longer just a dream, but a vision to strive for as rapidly as we can.

Management Innovations

NIH has an enormous and growing scope of mission. We conduct or support research on over 6,600 diseases and conditions, from the most common to the rarest. In 2005, more than 43,000 research grant applications went through our rigorous two-tiered review process, with about 22 percent of applications ultimately receiving funding.

More than 80 percent of the NIH budget supports extramural research at 3,100 institutions around the world, employing about 200,000 scientists and other research personnel. Another 10 percent of the budget goes into the NIH intramural program, consisting of approximately 6,000 scientists, where work is focused on public health priorities and cutting edge research. The hub of the intramural program, the NIH Clinical Center on the Bethesda campus, is the world's largest dedicated clinical research complex.

NIH is spending **$95 per American** this year on medical research, and we need to make every dollar count. With the growth and increasing complexity of the agency, NIH has aggressively moved to transform its management strategies and decision-making processes. To streamline, harmonize and better coordinate decisions that affect the entire agency, in 2003, I established the NIH Steering Committee, composed of nine Institute Directors who serve on a rotating basis. Six working groups support the Steering Committee. This new governance structure has enabled greater coordination and harmonization between the 27 Institutes and Centers at NIH.

NIH has addressed the need for more robust means to oversee the vast NIH research portfolio, and plan and launch trans-NIH initiatives. While the NIH successfully developed important trans-NIH initiatives such as the Roadmap for Medical Research, the Strategic Plan for Obesity Research, and the Neuroscience Blueprint, the agency is now implementing even more rigorous and transparent processes and developing cutting-edge tools to analyze, assess and manage the array of research it supports. This will provide better information to support planning and priority-setting in areas of shared Institute and Center interests. To reinforce these accomplishments, NIH is establishing a new office within the Office of the Director—the Office of Portfolio Analysis and Strategic Initiatives (OPASI).

Review of our programs by the Office of Management and Budget under the congressionally mandated Government Performance and Results Act (GPRA) provides

evidence that our programs are effective. We have been rated in the top 15 percent of federal organizations.

NIH's effective performance is reflected in recent scores as measured by the OMB Program Assessment Rating Tool (PART). In the FY 2007 PART, the Buildings and Facilities Program and the Intramural Research Program both received the highest possible rating of *effective, with scores of 96 percent and 90 percent, respectively*. On the FY 2006 PART, the NIH Extramural Research Program achieved a similarly high 89 percent. These high scores demonstrate exemplary management and substantial progress toward meeting NIH performance measures. To date, approximately 90 percent of NIH's budget has been PARTed and rated *effective*.

Translating Discoveries into Better Medical Treatment

Rapidly translating our discoveries from the bench to the bedside is a top priority of the NIH. The opportunities have never been greater to use modern research methodologies such as genomics, proteomics, metabolomics, high sensitivity biochemical methods and other novel strategies to bring new insights to the study of human populations and more rapidly achieve the goal of making medicine ***predictive, personalized and preemptive***.

To accelerate progress, NIH recently introduced the institutional Clinical and Translational Science Award (CTSA). The CTSA program will stimulate institutions across the country in transforming Clinical and Translational Science in the U.S.A. to (1) captivate, advance, and nurture a cadre of well-trained multi- and inter-disciplinary investigators and research teams; (2) create an incubator for innovative research tools and information technologies; (3) synergize multi- and inter-disciplinary clinical and translational research; and (4) accelerate the application of new knowledge and techniques to clinical practice at the front lines of patient care.

Training a New Generation of Scientists

New visions require new talent. In times of constrained budgets the most important action NIH needs to take is to preserve the ability of young scientists with fresh ideas to enter the competitive world of NIH funding. To that effect, NIH has launched the new "Pathway to Independence" program which will support, for each of the next five years, 150 to 200 recently trained scientists conducting independent, innovative research.

In Summary

Our Nation's investment in biomedical research has dramatically improved health outcomes. The return on the investment of the American people at NIH is nothing short of spectacular. Thanks to the support of Congress, we are able, through our science, to respond in record time to emerging threats such as SARS, Pandemic Flu and biodefense needs. We have learned how to decrease the incidence of many diseases and other disabilities for old and young Americans. The estimated total cumulative investment at the NIH per American over the past 30 years including the doubling period is about

$1,334 or about **$44 per American per year** over the entire period. In return, Americans have gained over six years of life expectancy and are aging healthier than ever before.

The President and Congress have wisely invested in biomedical research. We are acutely aware that NIH research is often the only hope for millions of people afflicted by disease. In the battle for health, NIH also believes that it needs to accelerate the pace of progress, as it is only through a fundamental transformation of medicine that solutions to the rising burden of healthcare will be found.

I will be happy to answer any questions you may have.

Elias A. Zerhouni, M.D.
Director, National Institutes of Health

NIH Director, Elias A. Zerhouni, M.D., leads the nation's medical research agency and oversees the NIH's 27 Institutes and Centers with more than 17,000 employees and a fiscal year 2004 budget of over $28 billion.

The NIH investigates the causes, treatments, and preventive strategies for both common and rare diseases helping to lead the way toward important medical discoveries that improve people's health and save lives. More than 80% of the NIH's funding is awarded through almost 50,000 competitive grants to more than 212,000 researchers at over 3,000 universities, medical schools, and other research institutions in every state and around the world. About 10% of the NIH's budget supports projects conducted by nearly 6,000 scientists in its own laboratories, most of which are on the NIH campus in Bethesda, MD.

Dr. Zerhouni, a well-respected leader in the field of radiology and medicine, has spent his career providing clinical, scientific, and administrative leadership. President George W. Bush nominated him to serve as the 15th Director of the National Institutes of Health, and he began in May 2002. Since then, Dr. Zerhouni oversaw the completion of the doubling of the NIH budget; initiated a strategic vision for the agency called the NIH Roadmap for Medical Research; established an NIH-wide research initiative to address the obesity; accelerated efforts in health disparities research; championed public access to NIH-funded research results; supported the Neuroscience Blueprint; streamlined NIH's executive decision-making process; and named nine new Institute and Center Directors, and filled many other senior-level positions.

Prior to joining the NIH, Dr. Zerhouni served as executive vice-dean of Johns Hopkins University School of Medicine, chair of the Russell H. Morgan department of radiology and radiological science, and Martin Donner professor of radiology, and professor of biomedical engineering. Before that, he was vice dean for research at Johns Hopkins. He became a member of the National Academy of Sciences Institute of Medicine in 2000.

Dr. Zerhouni has won several awards for his research including a Gold Medal from the American Roentgen Ray Society for CT research and two Paul Lauterbur Awards for MRI research. His research in imaging led to advances in Computerized Axial Tomography (CAT scanning) and Magnetic Resonance Imaging (MRI) that resulted in 157 peer reviewed publications and 8 patents.