



U.S. Senate Committee on Appropriations

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**U.S. Senate Appropriations Subcommittee on
Labor, Health and Human Services, Education, and Related Agencies
Testimony of Elias A. Zerhouni**

WASHINGTON, D.C. . The U.S. Senate Appropriations Labor, Health and Human Services, Education, and Related Agencies Subcommittee on Monday held a hearing to examine the proposed Fiscal 2008 budget for the National Institutes of Health. As part of that hearing, the subcommittee heard testimony from Elias A. Zerhouni, M.D., Director, National Institutes of Health. His testimony is below.

Good afternoon, 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 of \$28.9 billion for Fiscal Year 2008, and to discuss the priorities of NIH for this year and beyond.

I would first like to thank the Committee for your longstanding support of NIH, including in the FY 2007 Joint Resolution that provided additional support.

INTRODUCTION

The 21st century will be for the life sciences what the 20th century has been for the physical sciences. Mastery of the biological world will impact not just health, but also our ability to develop sensitive solutions to environmental and energy challenges and will be a key determinant of national competitiveness. One of the greatest challenges facing our society is the unsustainable growth rate of healthcare expenditures. NIH and its scientists deeply believe that we are in a transformative phase of the biomedical and behavioral sciences, where opportunities for discoveries and their translation have expanded considerably. We believe that we are on a path to transform medicine from the current practice of intervening often too late in a disease process, to a new era when medicine will be more predictive, personalized and preemptive, through a broader scientific understanding of the fundamental mechanisms that lead to disease years before it strikes the patient. In a relatively constant budget, we made the tough but necessary choices to ensure that the investment and momentum of biomedical research continues.

A more predictive, personalized and preemptive form of medicine is no longer just a dream but a vision to strive for, because it can reduce disease burden and its costs while improving individual quality of life.

Last year, I discussed the return on the Nation's investment in biomedical research. Today, I will highlight some of the progress we've made in the last 12 months and where we must be in the future to create a sustainable environment for the discoveries needed to transform people's health.

THE IMPACT OF PAST NIH RESEARCH

NIH-supported research of the past several decades has contributed to dramatically improved health outcomes across many diseases and conditions. For instance, we have made remarkable advances in coronary heart disease, the leading cause of death in the United States for the past 80 years. Were it not for ground-breaking research on the causes and treatment of heart disease, supported in large part by NIH, heart attacks would still account for an estimated 1.6 million deaths per year instead of the actual 452,000 deaths experienced in 2004. Our Nation has had particular success in reducing fatal heart disease in women. In February of this year, NIH's National Heart, Lung and Blood Institute announced that the number of women who died from heart disease decreased by nearly 18,500 deaths from 2003 to 2004. Part of this success is attributed to NIH's efforts to increase awareness among women that heart disease is their number one killer.

The mortality rates of cancer, the second-leading cause of death in the United States, have been steadily falling. This year, for the second year in a row, the absolute number of cancer deaths in the United States has declined despite the growth and aging of our population— a truly unprecedented event in medical history. More effective therapies have also led to improved outcomes for more than 10 million American cancer survivors. In 2006, new clinical guidelines were announced for the treatment of advanced ovarian cancer. And for another of our most deadly cancers, melanoma, a new gene therapy approach resulted in sustained regression of advanced disease in a study of 17 patients, whose own white blood cells were genetically engineered to recognize and attack cancer cells.

Nearly 21 million Americans have diabetes, a disease that can damage 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, and we would have many more cases of the dreaded complications of diabetes, including blindness and end-stage kidney disease. Our research has shown the enormous benefits to be gained by tightly controlling blood glucose levels in diabetes. The NIH-funded Diabetes Control and Complications Trial confirmed that individuals with diabetes can cut their risk for nerve disease by 60%, and half their risk for kidney disease and cardiovascular disease by intensively controlling their blood glucose levels. Our diabetes research has also shown that tight glucose control can slash the risk for eye disease by more than 75%— a critical

finding for the estimated 24,000 Americans who lose their sight to diabetes each year. In fact, diabetic retinopathy is the leading cause of blindness in adults under age 65.

The treatment of cognitive decline and mental disorders continues to improve at an incredibly rapid pace. In 2006, NIH supported the development of new strategies that helped depressed patients become symptom-free and prevented disease recurrence in older adults with single-episode depression.

Other noteworthy advances from 2006 included the development of promising new drugs for tuberculosis, inflammatory disease and muscular dystrophy, as well as exciting experimental results of vaccines against increasingly dangerous staph infections and against the H5N1 avian flu virus. Last year we also launched a trial for a new and promising vaccine against HIV/AIDS, and just last month, our scientists discovered a unique molecular weak spot in the armor of the HIV virus, which could have profound implications for vaccine development.

In brief, thanks to the Nation's investment in biomedical research, we have learned to diminish the harmful impact of many diseases and disabilities for all 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. Over the same time period, Americans have gained over six years of life expectancy and are aging healthier than ever before. New industries such as biotechnology, based on NIH-funded discoveries, have led to the creation of thousands of companies in the life sciences with impact beyond health. The American people's return on their investment in NIH is truly spectacular.

CURRENT CHALLENGES

In short, the many scientific advances achieved by NIH-funded researchers— over many decades— now allow our population to live longer and healthier lives. But as our population continues to age, a striking change becomes evident. The burden of our Nation's health problems has dramatically shifted from acute to chronic diseases. Chronic diseases now consume over 75% of healthcare costs and continue to grow at a rapid pace. Profound lifestyle changes have led to the emergence of non-communicable diseases such as obesity and attendant growth in the prevalence of associated conditions, such as diabetes and heart, kidney and musculoskeletal diseases. It is important to note that the burden of these chronic diseases is not uniformly distributed among our population; health disparities remain a critical health issue that requires new and continuing efforts.

Let me now present a sobering reality. Despite medical progress, healthcare costs in the United States have risen to more than \$2 trillion, or about 16% of the Gross Domestic Product (GDP), and they grow at a rate greater than the GDP. The average amount spent on healthcare per person is about \$7,100 today. The causes of healthcare inflation are varied and complex, but it is clear that this growth rate is unsustainable in the long term and will impose an enormous burden on our people and

the competitiveness of our Nation. Biomedical research alone will not solve all of these problems, but it is an essential component toward a sustainable future. NIH and its scientists understand the need to reduce the impact of this great challenge through transformative discoveries and their rapid translation from laboratory to patients.

While seeking medical discoveries that will address ongoing concerns, we must also be prepared to confront new and unpredictable threats. Emerging and re-emerging infectious diseases are on the rise, as micro-organisms develop strategies for evading our best drugs. We face the rapid globalization of mass transportation and the staggering worldwide threat of HIV/AIDS and other familiar foes. We must stand ready for the threat of pandemic influenza and of man-made bioweapons for which we have greatly expanded our investments in the past several years. Addressing these many new threats will require sustained scientific efforts and further breakthroughs.

STRATEGIC VISION FOR THE FUTURE: From curative to preemptive medicine

Historically, medicine has been reactive, and patients did not seek attention until an acute event required them to seek a doctor's cure. Our system of care is based on managing these late events on an episodic basis— an increasingly costly and unsustainable approach. What then is the scientific vision for change? Our goal at NIH is to usher in an era where medicine will be predictive, personalized and preemptive. This trend will also require a transformation in the fundamental relationship between healthcare providers and patients, necessitating continuous participation of individuals, communities and healthcare institutions as early as possible in the natural cycle of a disease process.

Based on NIH-supported research, we now know that many of the most prevalent diseases of our time begin silently, many years before they inflict their obvious damage to patients. Increasingly, we are able to identify biomarkers that are predictive of the likelihood of developing a serious condition later in life. Just in the past year, we have discovered genetic variations that help predict the development of age-related macular degeneration, a major cause of late-life blindness. We also discovered a new gene associated with Alzheimer's disease, a major control gene for diabetes and a marker of genetic susceptibility to prostate cancer. The genetic marker for prostate cancer risk came from the NIH-supported Cancer Genetic Markers of Susceptibility (CGEMS) study. Through the CGEMS database, genetic information about prostate cancer risk will be shared with cancer researchers across the country. The mining and sharing of genetic information will provide much-needed information to help us develop new strategies for the early detection and prevention of prostate cancers, which take the lives of nearly 27,000 American men each year and disproportionately affect African Americans.

Just consider, for a moment, how more predictive and personalized treatments could improve the safety and effectiveness of drugs. We know that 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 acquired thanks to 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.

As an example of emerging personalized medicine, cancer researchers have developed a test that helps to 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. The test has the potential to change medical practice by identifying tens of thousands of women each year who are unlikely to benefit from chemotherapy, sparing them from unnecessary and costly treatments and their harmful side effects. Such a test is now being readied for FDA review and is being evaluated in a long-term clinical trial sponsored by the NIH's National Cancer Institute.

Ultimately, this individualized approach completely different than how we treat patients today will allow us to preempt disease before it occurs. We have already benefited greatly from these insights. For example, we know that controlling blood pressure, cholesterol levels, weight and diet, and eliminating smoking, greatly reduce the risk of heart disease and lung cancer. Mortality from colon cancer has dropped because our scientists have shown that such cancers evolve from accumulated genetic mutations in initially benign colon polyps which, if removed, preempt the development of lethal cancers.

Because of a hundredfold reduction in the unit cost of genomic technology, we can now study, at affordable costs, the differences between patients who have a disease and their normal counterparts. These breakthroughs form the basis of our budget request for the continuation of the Genes, Environment and Health Initiative started in 2007 and strongly supported by Secretary of Health and Human Services Michael Leavitt, who is also championing the concept of personalized medicine across all of HHS. With this new initiative, we expect to uncover within three years the potential molecular causes of the 10 most common diseases afflicting the U.S. population. As part of this initiative, we will also launch a technology development effort that will enable scientists to measure many types of environmental exposures at the individual level.

Taken together, these studies will lead to better understanding of the environmental and genetic factors that affect the development of many diseases. Imagine that your heart rhythm, brain activity, blood pressure and many other variables could be remotely monitored through a device like your cell phone and sent to a secure web-based analyzer with direct access to experts and a modern health information system. Suppose, for example, that these technologies could identify dangerous patterns in your heart rhythms or key biomarkers and warn you of an impending heart event or stroke or other complications. Imagine your doctor could tell based on your genes whether you need to take preemptive action to thwart a costly or painful disease, or whether you

can avoid taking expensive medications for life because you are not at risk. This is not some science fiction. NIH is supporting the development of that future today.

MAINTAINING MOMENTUM TOWARD 21ST CENTURY MEDICINE AND HEALTH

Building toward the future involves innovations in multiple areas, including technology, research and training paradigms, information interoperability, and greater knowledge and resource management. We have seen an explosion of new discoveries and novel opportunities for progress across all areas of science- from the most basic discoveries to the sequencing of the human genome, to the development of fields that simply did not exist a few years ago. These emerging fields include proteomics, computational biology, or more recently the discovery of RNA interference, for which two NIH-funded scientists- Drs. Craig Mello and Andrew Fire- received the 2006 Nobel Prize in Physiology or Medicine.

The greatly expanded scope of research and new health challenges have necessitated a dramatic expansion of the Nation's research capacity, which was a primary outcome of the doubling of the NIH budget. This remarkable growth in research capacity was accomplished by leveraging NIH resources with private sector resources to nurture more investigators, develop new technologies and build infrastructure.

The United States is now the preeminent force in biomedical research, and continues to lead the highly competitive biotech and pharmaceutical sectors, but it is also the focus of increasing challenges from government-supported research in Europe and Asia. NIH basic research and training programs produce steady streams of novel discoveries and innovative people that flow into our industries, making them more competitive. Multi-national corporations often choose to set up facilities here, to tap into the American pool of talent and research nexus, both largely developed through NIH funding.

NIH-funded research leads to patents and spin-off companies across the Nation. Through the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, NIH helps to support entrepreneurs, as they bring to the international market products that improve health and help to maintain American economic leadership. Thus, NIH research and training dollars leverage state and private investment, resulting in powerful academic research centers and entire geographic regions for greater creativity and productivity.

The American health research enterprise now has the capacity to achieve extraordinary medical advances and economic benefits for the Nation, and we must continue this momentum. We must sustain the capacity we have worked so hard to build and harness its potential.

The talented scientists and institutions we have nurtured are stepping up to the challenge. For example, NIH now receives twice as many applications for grants than before the doubling of its budget. Due to the marked competition for funds across so

many novel areas of research and health challenges, competition for grants and the quality of projects submitted to NIH is better than ever. We anticipate that the FY 2008 budget will again support about one-fifth of applications submitted, as opposed to one-third in FY 2003. We focused our budget request on maximizing the number of competing grants for new and established scientists. To encourage innovation and sustain the next generation of scientists to the greatest extent possible, we have also developed programs for new investigators and for pioneering high-risk/high-impact investigator-initiated research, the mainstay of fundamental discoveries.

To achieve our vision of modern medicine, we also need research scientists with broad expertise, from widely varied disciplines, coming together in highly cooperative and efficient teams to answer ever-more complex questions. To this end, NIH recently changed a long-held policy of having only a single principal investigator on any NIH grant to a new policy that allows, when appropriate to the science, multiple principal researchers to apply for a grant together. This new policy is encouraging collaboration across disciplines and enabling academic scientists to exercise creative leadership in a project while bringing more of the best and brightest from physical, biological and behavioral sciences to the task of solving the multifaceted and complex health-related problems.

As biomedical research becomes more comprehensive, and we recognize that complex diseases come under the purview of more than one or a few NIH Institutes and Centers, we have been stimulating collaborative endeavors through multiple trans-NIH activities, such as the NIH Roadmap for Biomedical Research. These trans-NIH activities focus on providing the impetus and support for high-risk/high-impact research through Pioneer Grants; developing tools and new scientific teams for furthering our understanding of the complexity of biological systems; and stimulating a large effort to re-engineer the Nation's clinical and translational research enterprise to support more effective interactions between laboratory research and its clinical translation.

In 2006, we launched the Clinical and Translational Science Awards (CTSA) Program, which is the first in-depth redesign of our system of applied research in 50 years. The CTSA Program is stimulating research institutions to foster more productive collaboration among investigators in different fields. The program also encourages creative organizational models and programs for training the next generation of clinician scientists, without whom much basic research cannot be applied to human populations. Ultimately, patients will be better served because new prevention strategies and treatments will be developed, tested and brought into medical practice more rapidly.

In addition, the NIH Intramural Research Program is launching several initiatives to make even more effective use of the highly talented scientists and state-of-the-art resources in our federal laboratories.

We have made every effort to generate greater synergies between NIH Institutes and Centers. For example, the NIH Strategic Plan for Obesity Research was launched in 2003 and involves 19 Institutes. The Neuroscience Blueprint brings together 15 NIH

Institutes and Centers and the Office of the Director, pooling resources and expertise to confront challenges in neuroscience research that transcend any single Institute or Center.

NIH is also taking advantage of emerging information technologies and is making management changes in response to public health needs. We are working to modernize our governance and improve efficiency. For example, the Office of Portfolio Analysis and Strategic Initiatives (OPASI) is developing a new knowledge management-based system, which performs text mining on NIH projects for more efficient research portfolio analysis. This tool will provide our Institutes and Centers with the information needed to more effectively manage their large and complex scientific portfolios, identify important emerging scientific opportunities and public health challenges, and target investments to those areas. OPASI will be invaluable for supporting key trans-NIH initiatives being incubated through the NIH Common Fund, which is a central feature of the NIH Reform Act of 2006.

We would like to take this opportunity to thank Congress for passing this landmark legislation, which will enable NIH to modernize its organization; incubate innovative ideas and potentially ground-breaking research; address emerging areas of scientific opportunities; stimulate support of cross-cutting science; and encourage collaborative efforts while preserving the ability of Institutes and Centers to continue their outstanding record in fulfilling their specific missions. We are diligently working to implement this legislation.

BUDGET PRIORITIES: Nurturing a New Generation of Scientists and Sustaining Innovation

New visions require new talent. One of NIH's highest priorities will be to preserve the ability of new and junior scientists with fresh ideas to enter the competitive world of NIH funding. We plan to use the additional funding provided to NIH in the FY 2007 Joint Resolution on these valuable initiatives. In FY 2007 and 2008, we will make every effort to maintain an average yearly number of approximately 1,500 new investigators receiving their first NIH R01-equivalent grants to create the vital next generation of scientific leaders.

Also in FY 2008, the NIH budget proposes to continue to grow fresh talent through the new "Pathway to Independence" program and to support 175 recently trained scientists in their quest to become independent researchers at an earlier point in their careers. These efforts, however, cannot come at the expense of the need to provide continuing support to our most productive and already established scientists. History shows that no one can predict from whom and from where the next great discovery or life-saving breakthrough will occur. It is therefore critical that NIH maintain a large variety of approaches to science and continue to work hard to encourage diversity among its scientists across all strata of our society.

We also strive to maintain the historical balance between the critically important investigator-initiated research portfolio and agency-driven priorities. Our successful model of research is based on creative and unconstrained scientists who propose their best ideas, so we can subject those ideas to rigorous and independent peer review, and then support the most promising and high-quality projects. Our budget targets resources to providing as large a number of competing Research Project Grants for individual scientists as possible. To support our vision and initiatives in the current budget environment, we made difficult but strategic decisions, like maintaining the average cost for competing grants at the FY 2007 level and not providing inflationary increases for direct reoccurring costs in non-competing grants. Our budget also proposes to reduce intramural research expenses.

Our basic science projected percentage in FY 2008 is 54.1%, and applied science is projected at 42.1%. The percent of NIH's budget designated for infrastructure support will increase slightly in FY 2008, to 3.2%. In total, the budget provides \$144 million to enhance our infrastructure stewardship to provide robust, modern, energy-efficient, and environmentally safe and secure facilities to conduct basic and clinical research.

SUMMARY

In closing, let me emphasize- we are at a critical point in biomedical research and must maintain the momentum to reach our vision. The opportunities for significant advances exist on virtually every front. We must not let these opportunities slip away. We do not want to lose the scientific capacity that we have developed in the recent past across the entire country. The transformation of health and medicine from the curative paradigm of the past to the preemptive paradigm of the future is within our grasp. As an example, in the past year alone, we realized a huge victory against cervical cancer, a disease that affects hundreds of thousands of women worldwide- a victory that we only dreamed about 10 or 15 years ago. The discoveries of Drs. Doug Lowy and John Schiller of NIH's National Cancer Institute on the human papilloma virus and the hard work of our private-industry partners have led to the development of the first FDA-approved vaccine against cancer. This is the kind of preventive intervention that will help us transform medicine in this century. The development of this vaccine represents just a small example of the NIH contribution to biotechnology and its transfer to the bedside- in this case before the bedside+is ever needed.

We are also working to preempt disease through evidence-based education that draws on the best behavioral and social science research. Let me give you just one of the many examples of how NIH translates research results into practical health interventions for the public. In 2005, NIH launched the WE CAN (Ways to Enhance Children's Activity & Nutrition) program. WE CAN is a behavioral intervention at the level of communities aimed at preventing childhood obesity. The overwhelming response from around the country has been gratifying. In less than two years, individuals and groups- ranging from schools and youth organizations to community and recreation centers- have joined with NIH and our partners in 36 states to energize

WE CAN. This is what I mean when we talk about the necessary participation of communities and individuals in their own health in a future redesigned healthcare system.

NIH also continues to expand its outreach and participatory efforts through its website, one of the most-visited in the world. The NIH website averages about 47 million visits each month, with more than 330 million page views.

I ask you to consider the challenges and the opportunities before us today in medicine and health, and the essential role of biomedical research. We have the key elements in place for overcoming a host of diseases and conditions and their societal burden, and momentum is on our side. Our research efforts have ushered in revolutionary changes in the diagnosis, treatment and prevention of disease. Sustaining the pace of biomedical discovery is essential to realizing a true and necessary transformation of medicine and health in our country.

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

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