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DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2008

MONDAY, MARCH 19, 2007

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 1 p.m., in room SH–216, Hart Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin and Specter.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF HON. ELIAS A. ZERHOUNI, M.D., DIRECTOR

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. The Subcommittee on Labor, Health and Human Services, Education, and Related Agencies will come to order. I welcome you today to the hearing on the fiscal year 2008 budget for the National Institutes of Health.

Whenever I talk about NIH, it is always a pleasure to sit with my good friend Senator Specter, who will join us very shortly. Maybe I should wait till he gets here so he can hear all the good things I've got to say about him.

But I'll just say that no one has fought harder to improve biomedical research in this country. He and I worked in lockstep to double funding for NIH between fiscal years 1998 and 2003, covering two different administrations. I always say it's one of my proudest accomplishments in my entire career in the Senate. I know he shares my disappointment that the NIH has fallen on tougher budgetary times since then.

The fiscal year 2007 joint funding resolution that Congress passed a few weeks ago brought some good news. We increased NIH funding by $637 million, enough to launch the National Children's Study. We added another 500 research grants and provided additional funding for high-risk grants and young investigators.

Even with that increase, however, fiscal year 2007 marked the fourth year in a row that NIH funding failed to keep up with the cost of inflation. In fact, since the end of the doubling period in fiscal year 2003, NIH funding has dropped by about 8 percent in real terms. That cut threatens to squander our Nation's investment in

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biomedical research, delay new cures and treatments, and discourage the next generation of young investigators from entering the field.

The President's fiscal year 2008 budget would make matters even worse. On paper, it would seem to cut NIH funding by $328 million. But the actual reduction is about $200 million more, so a total of about $529 million, because, under this budget, NIH would pick up the entire tab for the Global AIDS Fund, rather than sharing it with the State Department.

So, as a result of this, comparable funding for the National Cancer Institute would drop by $79 million, funding for the National Heart, Lung, and Blood institute, by $36 million, and the National Children's Study, which we just launched, would be stopped cold. I'm not ever in the habit of ever speaking for my good friend Senator Specter, but I think I can say we will not allow those cuts to take place.

This is the first of six budget hearings on NIH that this subcommittee will hold this spring. At today's hearing, we'll hear first from Dr. Elias Zerhouni, the Director of NIH. Our second panel today will consist of four leading scientists who have received NIH grants. They will discuss the impact of Federal funding on their areas of research, and why it's so important to increase our investment in NIH. All four of these scientists helped produce a new report on NIH, which I got last week, and it's entitled, "Within Our Grasp—or Slipping Away? Assuring a New Era of Scientific and Medical Progress." So, we're going to be discussing that in our second panel. This report will be released at a press conference immediately following this hearing.

Next Monday, we'll hold a hearing with the directors of five NIH institutes: NINDS, NIDA, NIAAA, NIMH, and NIDCD. Before the spring is over, the subcommittee will hear from the directors of each institute and center at NIH.

So, that's the agenda. Before I introduce Dr. Zerhouni, I'll yield to my good friend Senator Specter.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Thank you very much, Mr. Chairman.

This is a very important hearing by this subcommittee to hear from the director of the National Institutes of Health, our premier health agency in the United States, and he's the number-one administrator. Health is our most important capital asset. Without health, there is nothing any of us can do. I can attest to that, personally, from the medical problems that I have worked through.

In 1970, President Nixon declared war on cancer, and, had that war been pursued with the intensity of our other wars, my chief of staff, a beautiful young woman, 48 years old, Carie Lachman, wouldn't have died of breast cancer. One of my best friends, a very distinguished Federal judge, Judge Edward Becker, wouldn't have died last year from prostate cancer. We all know, within our immediate circle of friends and family, of fatalities which have occurred because of the maladies of one sort or another. It is within reach to cure cancer, to find ways on a breakthrough on Parkinson's and Alzheimer's and heart disease and juvenile diabetes, and the other maladies, with sufficient funding.

Senator Harkin and I, who have transferred this gavel with seamless efficiency from time to time, have worked on this matter together for decades, and we've taken the lead to increase in funding, sometimes on an annual basis in excess of $3 billion, to do the job. Well, it is simply unacceptable to have a $500+ million cut in NIH funding, as proposed by the administration this year. When you have a Federal budget of $2.9 trillion, an enormous sum of money, this large hearing room insufficient to stuff $10,000 bills into it to make, to make that kind of funding, to have an allocation of less than $30 billion, candidly, is scandalous. In an era when we are beset in the Congress all the time on how to reduce healthcare costs from the smallest of businesses to individual families to the biggest corporations, and the best way to reduce healthcare costs is to eliminate these major maladies, to prevent illness. We are blind, really, to this very, very, important objective.

Earlier today I called Dr. Zerhouni and asked that he focus on the issue of cost savings. That seems to be an item which has special appeal on Capitol Hill. Elimination of disease, and the suffering that goes with it, ought to be our primary concern, but somehow if it saves dollars, it attracts more attention.

We also have the issue of stem cell research which we've been fighting. We found out about stem cells, and their potential, in November 1998, and, within 10 days, this subcommittee held a hearing, and we've since had 20 hearings. Stem cells have the potential to be a veritable fountain of youth. We, regrettably, cannot use Federal funding on stem cell research, except for a few lines, which were available back on August 9, 2001. But if these embryotic stem cells were to be used to create life, no one would want to use them for research, but there are 400,000 available, and they're going to be discarded unless they're used to save lives.

Here again, Senator Harkin and I took the lead to appropriate $2 million for adoption, and a few have been adopted, but a very few, in the range of 100, contrasted with 400,000, which will be thrown away. So, our work is cut out for us.

You have two strong allies in Senator Harkin and myself, Dr. Zerhouni, and you have the potential to have 533 more if there's sufficient political pressure brought to bear on Washington, DC. I've talked about a million-person march on the Mall. A million people could be heard in the living quarters of the White House. Attitudes are changed in Washington, with political pressure. With 110 million people affected, directly or indirectly by disease, that group of public opinion could write its own ticket. Senator Harkin and I want to be the scriveners.

Thank you, Mr. Chairman.

Senator HARKIN. Thank you very much, Senator Specter.

Dr. Elias Zerhouni has served as Director of the National Institutes of Health since May 2002. Prior to that, Dr. Zerhouni was the executive vice dean of Johns Hopkins University School of Medicine, chair of the Department of Radiology and Radiological Science, and Martin Donner professor of radiology and professor of biomedical engineering. Dr. Zerhouni received his medical degree from the University of Algiers School of Medicine, completed his residency in diagnostic radiology at Johns Hopkins.

I might just add that since May 2002, every report that we've gotten, every indication, all the people that we've talked to, both in NIH and out in the countryside, have basically reported that Dr. Zerhouni has done an outstanding job of leading NIH since he's been there.

With that we welcome you back to the committee, Dr. Zerhouni. Your statement will be made a part of the record in its entirety. They had set it for 5 minutes; I said boost it up to 10, and, if you need more than that, we'll give you more than that.

So, please proceed as you so desire.

SUMMARY STATEMENT OF HON. ELIAS A. ZERHOUNI

Dr. ZERHOUNI. Thank you very much.

It's my pleasure to appear before you, Mr. Chairman and Senator Specter. There couldn't be more passionate supporters of science and research than both of you. As I've worked with you over the past 5 years, I have to be, also, a witness to not only your passionate support, but also your profound understanding of what makes science, and what makes medical research, work, and why it is so important to the Nation.

I also would like to thank you and the committee for your personal support for the increased funding for NIH in 2007 and the focus that you have brought towards supporting the next generation of scientists, and making sure that we do not become stale in our research, that our momentum is kept, in terms of new breakthroughs.

What I'd like to do is attract your attention to the slide and give you a very short summary of the essence of where we think NIH as a whole is going and why we're directing our efforts into what we would call a new era in medicine.

VISION FOR THE FUTURE

We need to have a vision for the future as a country. I think it is absolutely clear that 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 our environmental and energy challenges, and will be, in my opinion, a key determinant of national competitiveness for the 100 years in front of us. It is important to sustain our momentum in that regard.

I'd like to, first, point out to you that NIH has been, and continues to be, a very, very productive investment for the American people. We are living longer and healthier. Let me give you some specifics.

For the second consecutive year, annual cancer deaths in the United States have fallen. This is an unprecedented event. This has not occurred in any other country. It has not occurred for the time that we've had records. The absolute number of deaths decreasing is happening at the same time that our population is increasing in number and aging, at the same time.

What has been the investment that each one of us has made in that regard, in the war on cancer? On average, each American has spent about $9 per year, from 1974 to 2004, to accomplish these re-

sults, which are still insufficient. The complexity of cancer is such that we need to accelerate our research, not slow it down.

If you look at heart disease, there's been a remarkable drop in mortality from heart disease and stroke. In 2004, for example, a drop in death for women with heart disease has dropped from 1 in 3 to 1 in 4. More importantly, as Senator Specter was pointing out, the economic value of this drop in mortality and morbidity is estimated at $1.5 trillion to $2.5 trillion per year. This is the kind of result that I think we can foresee for the future. What has been the investment? About per year per American for each year over the past 30 years.

More importantly, I think it is clear that disability is decreasing among older Americans. It has dropped by 30 percent in the past two decades. Life expectancy has risen to 78 years, up 6 years since 1974. What has been the average total investment per American per year at NIH? Only $44 per year for medical research.

I think we can say that NIH has been a good investment, and continues to see itself as the vanguard for changing—changing, not just how we cure disease once the disease has struck us, but how we really advance our research to make a profound difference in what I think is our concern today, and that is the challenge of rising U.S. health expenditures. Biomedical research must deliver, and NIH is poised to deliver.

If you look at the percent of GDP consumed by healthcare costs, and its upward curve, it is clear that this will be one of the greatest challenges facing our society, because this growth rate of healthcare expenditures is not sustainable in the long run.

Historically, medicine has been reactive, and patients did not seek attention until an acute event required them to seek a doctor's cure. But our system of care has been based on managing these late events on an episodic basis. Is there a better vision? Is there a way science can help the country tackle this problem? I think there is. When you look at the projection of doubling of our costs in 10 years, to $4.1 trillion a year, I think one cannot but feel that there is a real race against time to discover new ways of practicing medicine.

Let me be clear. If we practice medicine in 25 years the way we practice it today, we will have lost the game of the century. It is very important that we understand that. Is there a paradigm in the future that will change that? The answer is yes. We need to advance the science that will allow us to pre-empt disease.

PARADIGM FOR THE FUTURE

I think if you look at this chart, you can divide any disease into three stages. One is what we call the preclinical stage, the bottom yellow band, where people do not know that they have a disease. We may not know that someone has a disease, because chronic diseases, which are the dominant factor in our healthcare cost, can begin 20–25 years before they become clinically obvious. Then symptoms start to appear, and we can intervene at that time. This is what we call the tolerable or compensated phase of a disease. Last, but not least, is the uncompensated phase, where, typically, curative treatment tends to occur.

What we've done over the past 30 years is try to move back in time to try to address diseases before the critical phase. But, in the future, what we see with the advances we've made in the past 10 years is, that for the first time—the complexity of biology and the advances we've made in science tell us that we could start to understand disease years before it strikes by understanding the first molecular events that lead to disease and intervening at that time. The potential cost savings are enormous, because, as the white curve shows, costs increase exponentially with the typically late interventions that we today practice. It is much more expensive to take care of heart disease in the late stages than to try to prevent it with an intervention very early in the life cycle of the disease.

That is, in my view, the vision of the future. This is how NIH research can potentially provide new insights, which we do not have today. But it is clear that the opportunities are there. Our scientists are doing an enormous amount of work in discovering, every day, new targets to understand the complex diseases that harm our people. We need to maintain the momentum of that research.

Let me just show you an example here of a disease called rheumatoid arthritis. This is a patient's hands at early stage, middle stage, and late stage. How are we going to improve costs? How are we going to make a change in the natural history of this disease? Obviously, in the late stage, not much can be recovered, and managing that late stage is quite expensive. We've made progress over the past 10 years. There's a new class of antirheumatic drugs that dramatically slows disease progression by focusing on a factor called tumor necrosis factor and reducing the impact of that factor. But that is not enough. We really need to go earlier in the disease process. That's why, in 2006, for example, genetic discoveries have revealed new genes, which we didn't know about 3 years ago, before the—at the end of the doubling of the NIH budget. The completion of the human genome in 2003 has allowed us to accelerate this kind of discovery. But every time we find a gene, that means more research has to be done on that gene, because the gene is only the code of what may be wrong in that disease. Much more research lies ahead of the discovery of a gene. Therefore, it is important for us to see that this research continues so that, in the future, we will pre-empt by intervening on the very fundamental factors that lead to that disease, and hopefully eliminate the costs of that disease.

4 P'S—PREDICTIVE, PRE-EMPTIVE, PREVENTIVE, AND PARTICIPATORY

So, the future paradigm, if you will, if I can summarize it, is what we call the 4 P's.

One, using the new technologies we've developed, the new insights we've developed over the past 10 years, there is potential for us to be much more predictive about to whom, how, when a disease will occur. By using gene-chip technology, we can, today, do that in several diseases.

Second, treatments are going to have to be personalized. Every one of us is different, and we react differently to different therapies. That's the second P.

Third, we have—through that knowledge, we have to become preemptive. But this will also require a revolution in the way we conceive of healthcare. Instead of a disease-based healthcare system, or healthcare system driven by disease, we should focus on a healthcare system drive by health, where patients are not sick, patients are healthy when they come in contact with us. That will mean people will have to participate a lot more in their care than ever before. That means transformation of the healthcare system, driven by new science. This is what I call the Era of Precision Medicine. This is what we're working for. This is what NIH's vision has been, and continues to be. More importantly, we feel that we are at the edge of being able to do that.

PREPARED STATEMENT

NIH and its scientists deeply believe that we are in the transformative phase of the biomedical and behavioral sciences, where opportunities for discoveries and their translations—translation have never been greater. We believe that we're on the path to do that. We want to encourage not only the current generation of scientists, but the future generation of scientists, to come unhampered, and to be supported, because this is the race of the century. In the 21st century, no nation will prevail unless it prevails in the life sciences.

Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF DR. ELIAS A. ZERHOUNI

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 fiscal year 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 percent, 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 percent—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 6 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 percent 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 percent 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 fiscal year 2008 budget will again support about one-fifth of applications submitted, as opposed to one-third in fiscal year 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 fiscal year 2007 Joint Resolution on these valuable initiatives. In fiscal year 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 fiscal year 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 fiscal year 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 fiscal year 2008 is 54.1 percent, and applied science is projected at 42.1 percent. The percent of NIH's budget designated for infrastructure support will increase slightly in fiscal year 2008, to 3.2 percent. 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 word. 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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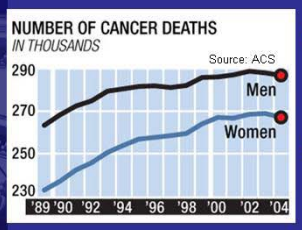
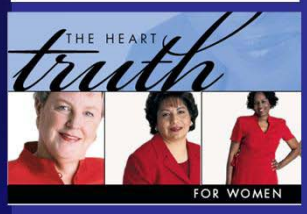
Due to Advances of Past 30 Years

Americans are Living Longer and Healthier



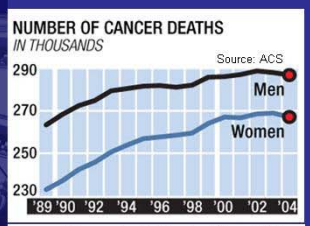


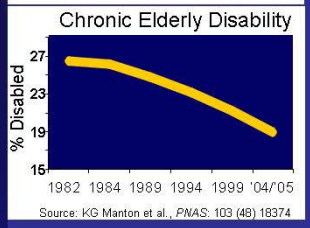
- For the second consecutive year, annual cancer deaths in the United States have fallen
- Over 60% drop in mortality for heart disease and stroke – in 2004, drop in deaths of women from Heart Disease from 1/3 to 1/4 reported

Heart disease investment per American
~$4/yr
1974-2004

Due to Advances of Past 30 Years

Americans are Living Longer and Healthier





- For the second consecutive year, annual cancer deaths in the United States
- Over lity for heart ke – in 2004, drop in deaths of women from Heart Disease from 1/3 to 1/4 reported
- Chronic disability among older Americans has dropped by 30% in the past 2 decades, and the rate of decline is accelerating
- Life expectancy rises to 78 years, up 6 years since 1974

Total NIH Investment per American
~$44/yr
1974-2004

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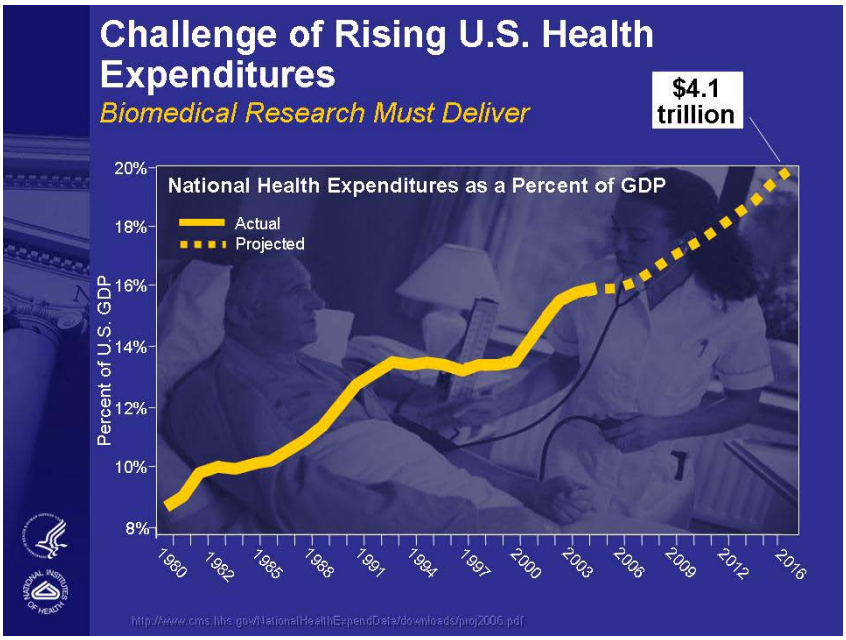

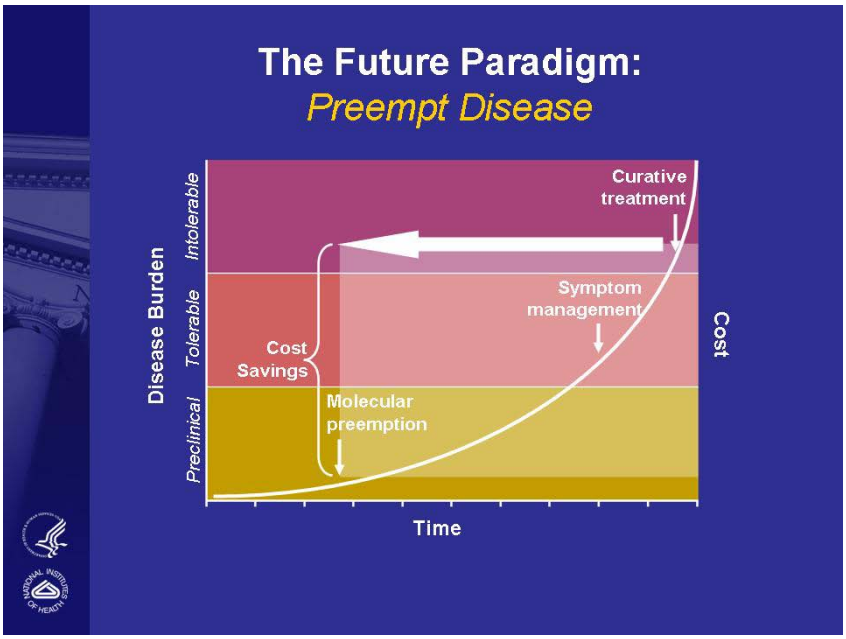

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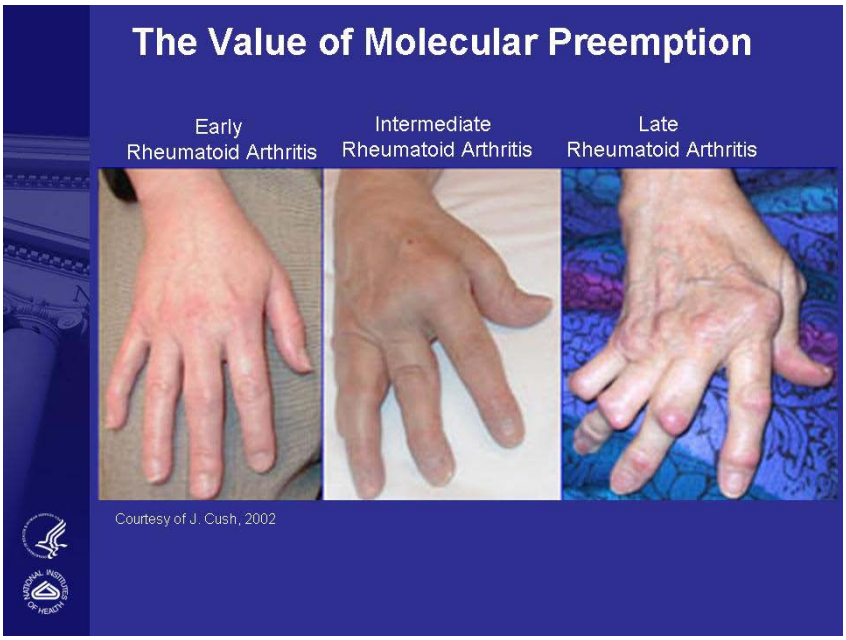

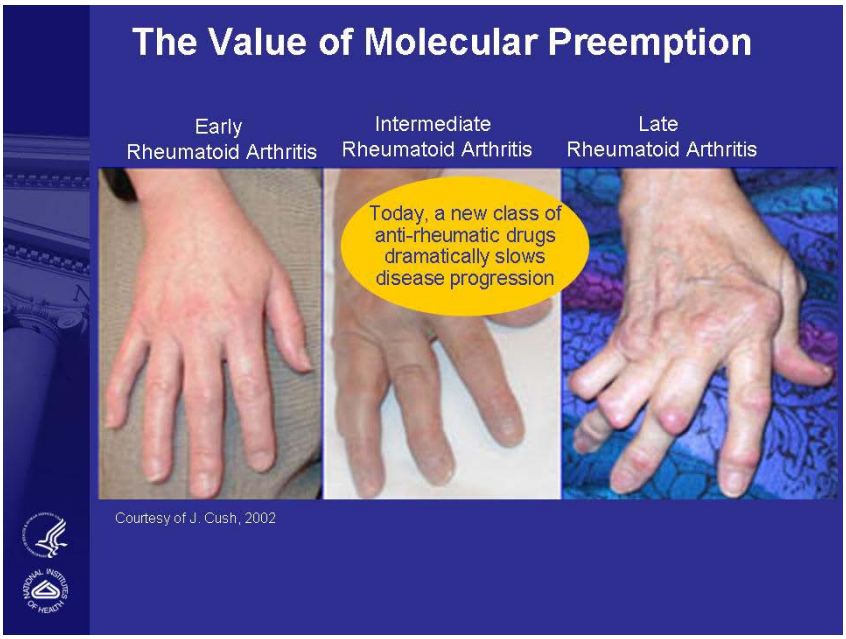

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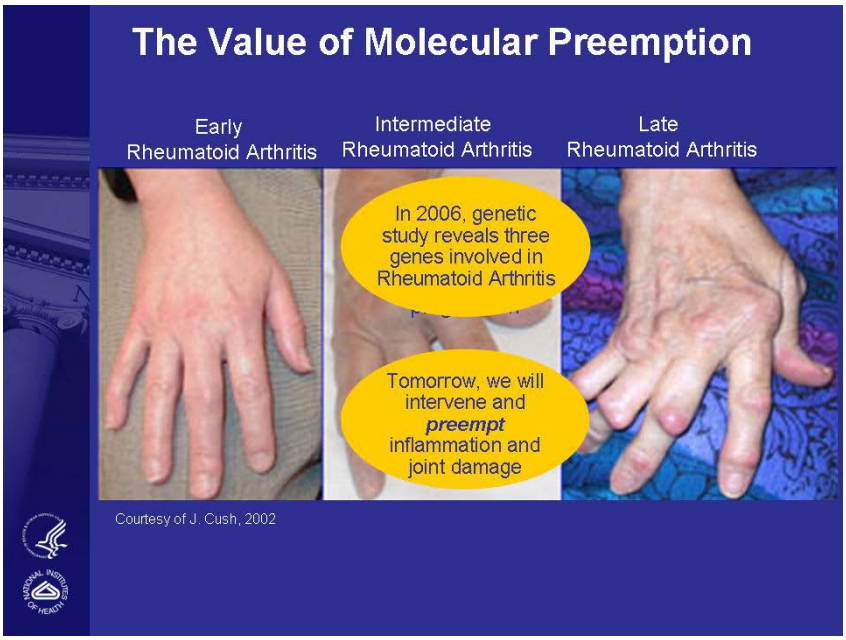

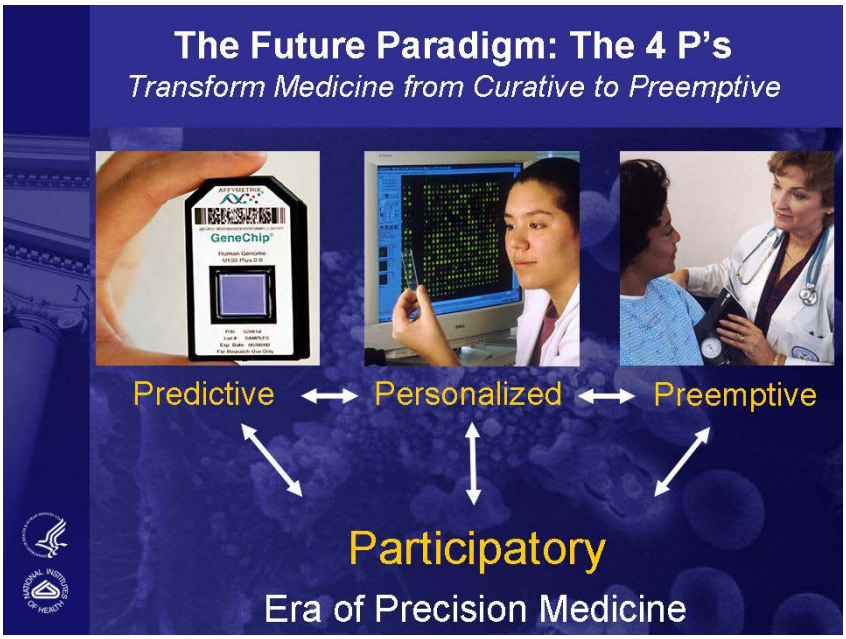

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Senator HARKIN. Dr. Zerhouni, thank you very much for a very enlightening and succinct presentation.

I've been fond of saying a lot in the past that in America we don't have a healthcare system, we have a sickcare system. When you get sick, you get care. There's not much up front to help keep you from getting sick. A statistic I saw recently was that 75 percent of all medical cost in Medicare is due to the treatment of chronic illnesses which have reached their later stages. So, a lot of these are preventable, if you get to them early on. That's what you're showing here, to get to a true healthcare system, where you keep people healthy in the first place.

So, I really appreciate that presentation. I think that's a good note on which to begin our questioning.

STEM CELL RESEARCH

Dr. Zerhouni, I have a series of questions, and then I'll yield to Senator Specter. We may go back and forth here for a while. But the first thing I want to get into is something that Senator Specter brought up. Both of us worked together on this, very hard. Senator Specter had the chairmanship during all those years when we first isolated embryonic stem cells, in Wisconsin, at the University of Wisconsin. Senator Specter had the first hearings on that. As he said, we've had 20 since then. He and I have worked together harmoniously on this to try to push the frontiers of this and to get around the restrictions.

But when you were appointed to your position 5 years ago, a lot of people were anxious about what we were going to do about embryonic stem cell research and about the restrictions that were placed on August 9, 2001, at 9 p.m. At that time, you know, there

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was a limit of how many stem cell lines could be financed through Federal funds for research. We were told, at that time, there were 78. But then, we've found out a lot since then.

Now, again, when you first came before this committee, you said you wanted to let science take its course. Well, over the last 5 years, science has taken its course. I thought that was profound on your part to do so, to say that, because what we've discovered is that those 78 lines are not 78, they're really about 21. At least that's the latest I've been told. Only a handful are used on a regular basis, limiting their genetic diversity. We know, also, that all of them have been contaminated, because they were grown on mouse feeder cells. So, the likelihood that they would ever be used for any human intervention is unlikely. We now know that there are much better ways of deriving and growing stem cells than what we knew in 2001. However, the lines derived from these new methods are not eligible for Federal funding.

So, given all that's happened in the last 5 years, I'd just like to revisit this issue with you. With everything you've told us about the vision for the future and getting in front of this, would scientists have a better chance of finding these new cures, new interventions for diseases, if the current restrictions on embryonic stem cell research were lifted?

Dr. ZERHOUNI. I think the answer is yes. My experience has been this. In 2001, I think the policy that was put in place was the first one to fund embryonic stem cell research. I think NIH has done a great job in the first 3 years of that in establishing infrastructure, funding new scientists, which weren't fundable before. Since 2004, I think it's very clear, from the point of view of science and what I have overseen, that these cell lines will not be sufficient to do all the research we need to do, for the reasons that you mentioned, but the most important one is that these cell lines have exhibited instability, from the genetic standpoint, and it's not possible for me to see how we can continue the momentum of science in stem cell research with the cell lines that we have currently at NIH that can be funded. So, from my standpoint, it is clear today that American science is—would be better served, and the Nation would be better served, if we let our scientists have access to more cell lines, because they can study with the different methods that have emerged since 2001, the different strategies that we now understand, underlie the fundamental issue, which is nuclear programming, or DNA programming, or reprogramming.

So, the answer is yes.

Senator HARKIN. Well, Dr. Zerhouni, let me ask you to comment on two things, then.

We're hearing a lot now in the popular press, not so much in the scientific journals, that we don't have to do this, that adult stem cells can take care of it all, then we have amniotic stem cells, and then we have umbilical cord stem cells, and that we don't need embryonic stem cells, that all these others will handle it, will take care of it.

Second, on the issue of stem cell research itself, why is it so important that NIH do this? Already, California is doing it. I think Missouri just passed a constitutional amendment on it. In Iowa, my own State, the legislature just voted, and the Governor signed a

law lifting the ban, in Iowa. Wisconsin, of course, New York. So, different States are doing different things. A lot of times when I talk about this, people say, "Well, if the States are doing it, there's no real reason for NIH to be involved in this." So, if you could address both—why is it important for NIH? What about adult stem cells and all these others being sufficient?

Dr. ZERHOUNI. Well, let me give you my point of view, and, I think, the scientific point of view here. Again, my statement that I—as I made 5 years ago, is that I will always stick to the scientific truth, and disease knows no politics. So, let me say this. The presentations about adult stem cells having as much, or more, potential than embryonic stem cells, in my view, do not hold scientific water, if you will. I think they are overstated. I think we do not know, at this point, where the breakthroughs will come from. I think scientists who work in adult stem cells, themselves, will tell you that we need to pursue, as vigorously, embryonic stem cells.

My point of view is that all angles in stem cell research should be pursued. I think people sometimes misunderstand what the fundamental challenge is in stem cell research. It's not solely to use it to replace things, like in adult stem cell transplantation, but it's to really understand, for the first time in the history of mankind, how DNA is programmed and reprogrammed. Well, to do that, you need to have copies of cells that have been programmed—adult stem cells—but also copies of cells that have never been programmed forward—embryonic stem cells. The key thing here is that the nation that understands that will be as—in the stronger position, as we were in the 20th century for the information revolution, for computers. It's basically the software of life that we're talking about. So, from my standpoint as NIH Director, it is in the best interests of our scientists and our science, our country, that we find ways, that the Nation finds a way, to allow the science to go full speed across adult and embryonic stem cells equally.

Senator HARKIN. Why is it so important for NIH?

Dr. ZERHOUNI. Right. So, why is it important? As the NIH Director, I can tell you that the role that NIH has played in this country over the years has been second to none. There is no State that can really provide the depth of oversight and stimulation of this research over the long run. This is not a 1-mile race; this may be a marathon. It is important, I think, for NIH to play its historical role. I think that we have done that. We can do this, with appropriate oversight, a lot of safeguards, to make sure that this research is not misused.

NIH'S LEADERSHIP IN STEM CELL RESEARCH

Senator HARKIN. Ethical guidelines.

Dr. ZERHOUNI. Ethical guidelines. You know, Senator, we've done this. We've done this with the Recombinant DNA Advisory Committee in 1976, 1977, 1978. At that time, as you know, genetic engineering came on the scene. There was a huge question about both the safety and the ethics of using genetic engineering. Well, NIH took the lead, and set up a Committee called the Recombinant DNA Advisory Committee. We've been probably the most successful country in biotechnology. We've created a completely new industry. I think that this is the kind of role NIH can play. If you have a

patchwork of policies, a patchwork of different approaches, you may not have the same standards. It will be very difficult for our country to muster its strength unless we have some sort of moving—of move forward in this area. We cannot, I think, be second-best in this area. I think it is important for us not to fight with one hand tied behind our back here.

Senator HARKIN. I also——

Dr. ZERHOUNI. NIH is key to that.

Senator HARKIN. I also see what's happening out there now in California, where they're in a bidding warfare to get scientists to come there. Missouri's now going to do some bidding. Wisconsin. I suppose Iowa will probably get in the game now that we've lifted the law. So, it just seems that—to me, anyway—by providing NIH with this authority, which—you have the experience, the oversight, you are the world's leader. Everyone recognizes NIH as being the gold standard of unbiased research—that if you put NIH's blanket over the thing, I think it would reduce, a lot, this kind of bidding warfare between States, and then we'd have a national kind of an approach on this. Plus, NIH could reach out to other countries and coordinate other countries in doing this research, also. Is that, sort of, the kind of process would take place?

Dr. ZERHOUNI. My view is that I think it's time to move forward on—in this area. It's time for the Nation's policymakers to find common ground to make sure that NIH does not lose its historical leadership. I think we've maintained that leadership all the way to 2004–2005. But, as we've discovered, the lines that we have are less viable than we would have liked them to be—as these lines are older, I think it's important to realize that we need to move forward here, and NIH needs to continue its historical role as the leader of biomedical research in the world. To sideline NIH on an issue of such importance, in my view, is shortsighted. I think it wouldn't serve the Nation well in the long run. We'd need to find a way to move forward. I look at—obviously——

Senator HARKIN. Yeah.

Dr. ZERHOUNI [continuing]. It's more than science that is involved here, but I hope that we can find that way forward soon.

Senator HARKIN. Well, Dr. Zerhouni, let me thank you for a very profound and courageous statement that you've made here today.

Dr. ZERHOUNI. Thank you.

Senator HARKIN. Thank you.

DECLINE IN CANCER DEATH RATE

Senator Specter.

Senator SPECTER. Dr. Zerhouni, as you have testified, the deaths due to cancer have declined in the last 2 years. To what extent would you attribute that to research done by NIH?

Dr. ZERHOUNI. It's difficult to figure out exactly what is contributing to what, but I can be somewhat specific. Most scientists look at this decrease and feel that the main cause has been the decrease in smoking, that behavioral changes—social and behavioral sciences have contributed to epidemiology and prevention a great amount. The second cause has been early screening. If you look, for example, at colon cancer, the rates of colon cancer, and the death rates, have come down. Why? Because we have promoted the early

detection of polyps. Now, how does NIH play into that? Well, it turns out that the discovery that told us that polyps are really the pre-emptable, the preventable cause of the cancer, was that the genetic changes that lead to cancer start with a polyp. So, it's a——

Senator SPECTER. So, it is the NIH research which has identified a way for early screening to treat cancer at an early stage.

Dr. ZERHOUNI. But the basic research——

Senator SPECTER. Is that correct?

Dr. ZERHOUNI. That is correct, Senator. The most important is the NIH basic research, the study—the findings of Dr. Vogelstein, for example, who discovered that cancer of the colon does not happen overnight, but happens through a cascade of genetic changes that start with a polyp. That's what then led to the development of screening, and its impact on the reduction of cancer rates.

Senator SPECTER. NIH has researched and found treatments for various strains of cancer, isn't that correct?

Dr. ZERHOUNI. Absolutely.

UNDERSTANDING CANCER

Senator SPECTER. How many strains of cancer are there? We talk about cancer as one generalized term, but approximately how many different strains of cancer are there?

Dr. ZERHOUNI. That's an excellent question, Senator. Most people will say 200 types of cancer are known. But my view is that, as I've followed this field very closely—is even within breast cancer, for example, there are many subtypes of breast cancer. So, if you look at cancer, it's not one disease, it's 200 separate diseases, and the molecular changes that occur in each one of them may actually be different from one to the other. This is why we need to do more research, to understand what's different between a cancer that kills and a cancer that doesn't, and how do you treat this one versus that one?

Senator SPECTER. We have had estimates, on prior hearings by this subcommittee, on how long it would take to cure Parkinson's. Would you say that it would be realistic to give an approximation as to what it would cost to cure cancer, and how long it would take?

Dr. ZERHOUNI. Very difficult to do that, as you know.

Senator SPECTER. Well, that's why I'm asking you, Dr. Zerhouni.

Dr. ZERHOUNI. I appreciate that, Senator. I think it's clear that if you look at the advances that we're making today, that the—the challenge in front of us is to understand the complexity of cancer treatments relative to the complexity of the biology of cancer. Most people would say that in the area of Parkinson's disease, for example, that there are—we need to make progress at the basic level to understand what are the—what is the first mechanism of disease. We have several mechanisms of disease that we are working on. As long as you don't know that, it's very hard to predict when you're going to cure Parkinson's disease. But we're already studying—knowing, for example, which genes are involved in Parkinson's disease. We've made discoveries that tell us that Parkinson's disease relates to abnormalities in the neurons. Some people think it's because there's accumulation of abnormal protein mechanisms. But

here is the answer. The answer is, I can assure you that with less research, the cure will take much longer than with more research.

Senator SPECTER. Well, that's a pretty obvious conclusion, Dr. Zerhouni——

Dr. ZERHOUNI. I know. Well, it's like the question——

Senator SPECTER [continuing]. But——

Dr. ZERHOUNI [continuing]. You posed, Senator.

QUANTIFY FUNDING DECISIONS

Senator SPECTER [continuing]. But what we are looking for, within reason, is finding some way to quantify it. Now, I've had some experience with Hodgkins, and I have been informed of a variety of advances in the treatment of Hodgkins. Different—they call it a cocktail—that wasn't my idea of a cocktail before I had Hodgkins—and they told me a complex categorization and various substances. I've talked to others, and the field has progressed tremendously. All for the better. What would be very meaningful, as we approach your budget, would be to try to get some way to quantify, as best you can—now, I know this is not going to work out to be a mathematical formula, but, when we talk about the various strains of cancer, it is important to know how many research projects are undertaken, and how many you are turning away.

We moved, on this committee, to appropriate very substantial sums over a 4-year period of time. From fiscal year 1999, we increased the budget to slightly under $2 billion—$1.950 billion. The next year, we appropriated the increase was $2.190 billion. The year following a $2.630 billion increase. The year following, an increase of $2.830 billion. The year following, an increase of $3.770 billion. So that we are able to increase funding over a 5-year period, some $13 billion.

Now, how did we do that? We took a budget in the range of $140 billion, which the subcommittee has, which funds three very important departments, Health and Human Services, Education and Labor and we pruned through the budget, found, with very sharp pencils, where we could establish priorities to increase the funding for NIH.

Now, you've testified, in the past, that increase in funding enabled you to grant many, many more applications for funding. More recently, we have seen a decrease. Senator Harkin and I had to fight like tigers last year to add a little over $600 million to stop a $50 million cut in the National Cancer Institute. Now, what catches the attention of our colleagues would be specifics. So, my request to you—and I've made similar requests in the past—is to go back and make an analysis, and give us your best judgment as to what is happening with the decrease in the funding. The President's budget now is more than $500 million below last year, without considering an inflationary increase. We would like to know what effect that's going to have on research, so that—tell us, number one, your best judgment as to what it would cost to cure cancer, or as close as you can to that analysis, taking the strains of cancer and how many research projects you need, and over what period of time; and then, second, what's going to happen to NIH if the budget is cut by more than $500 million. If you take an inflationary factor of 2 percent, it's several billion dollars that it's being cut.

Then, the third factor that would be very helpful would be to tell us what would be done by way of prevention. It's very expensive to treat somebody with Hodgkins. I can tell you that personally. Your statistics are also impressive when you say that the second year in a row there's been a 60-percent drop in mortality for heart disease and strokes. That means 60 percent fewer people have died. The drop in deaths of women from heart disease, from one-third to one-fourth, reported.

[The information follows:]

PROFESSIONAL JUDGMENT COST TO CURE CANCER

If I may: "What will it cost if we do not cure cancer?". The National Institutes of Health estimate overall costs for cancer in 2006 as $206.3 billion: $78.2 billion for direct medical costs (total of all health expenditures); $17.9 billion for indirect morbidity costs (cost of lost productivity due to illness); and $110.2 billion for indirect mortality costs (cost of lost productivity due to premature death).[1] Between 1974 and 2004, on average, each American has spent about $9.00 per year on cancer.[2] Moreover, economists at the University of Chicago, Graduate School of Business have estimated that a 1 percent reduction in cancer mortality would be worth $500 billion to current and future Americans. A "war on cancer" that would spend an additional $100 billion on cancer research and treatment would be worthwhile if it has a 1-in-5 chance of reducing mortality by 1 percent and a 4-in-5 chance of doing nothing at all.[3]

The primary focus of the NCI is on research and developing prevention and treatment options; it is necessary for others in the cancer community to ensure that the results of our efforts are disseminated and applied.

COST TO CURE CANCER

It is probably unrealistic to predict when cancer will be cured. Cancer is not one disease, but represents over 200 diseases and as a result is an exceptionally complex health care problem. Eliminating cancer as a significant burden will require stepwise gains in scientific knowledge and innovative ways for translation of this knowledge to the clinic. Progress is made by building upon pre-existing discovery, and the pace of scientific advances is, of course, driven by the amount of resources available for laboratory research and clinical translation. The NCI has never been at a more exciting place in terms of understanding the molecular mechanisms causing cancer and determining its progression. We have made tremendous progress over the last decade that has resulted in a measurable decline in cancer deaths for both men and women. Three decades ago there were 3 million caner survivors; today there are over 10 million.

What can also be said with certainty is that we are rapidly moving toward an era when cancer treatment will involve a molecular diagnosis of each tumor followed by highly personalized recipes of therapy. We are identifying the underlying genetic changes identified with the risk of developing cancer, we are increasingly able to detect cancer before clinical symptoms, we are learning how to use the immune system to keep cancer from progressing, and we are developing therapies that specifically target cancer cells. Using these combinations of approaches to prevention, diagnosis and treatment, we are beginning to see some cancers as manageable chronic diseases.

Of great concern is the knowledge that cancer incidence is 10 times greater for those 65 and older than for those under 65, and the death rate is 16 times higher. By 2030, 20 percent of the U.S. population will be over age 65 compared with 12 percent in 2004. Therefore, it is imperative that we maintain, if not accelerate, the momentum of scientific discovery.

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[1] American Cancer Society, Cancer Facts and Figures 2007.

[2] Congressional Transcripts, Congressional Hearings, March 19, 2007, page 5: Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Education and Related Agencies Holds Hearing on the Fiscal year 2008 Budget for the National Institutes of Health.

[3] Murphy KM, Topel RH: The value of health and longevity, J Political Economics: vol. 114, no. 5, pages 871–904.

BUDGET CUT BY MORE THAN $500 MILLION

The following examples illustrate what NIH can't do with the fiscal year 2008 President's Budget, relative to the fiscal year 2007 enacted level:

National Cancer Institute

Despite many fruitful studies on prostate cancer initiation and progression, the prostate cancer cell of origin has not been conclusively identified. **NCI will not be able to fund an R01 on the "Study of the Cell-of-Origin and Cancer Stem Cells in Prostate Adenocarcinoma" which seeks to identify the prostate cancer cell of origin—an understudied area in cancer biology.** In this highly focused application, the investigator would test the hypothesis that, in the prostate, there is a specific progenitor cell population that is sensitive to oncogenic transformation, and that this cell population is also responsible for hormone resistant prostate cancer formation. The application is innovative, timely, and likely to yield significant meaningful data that will drive the future of the field. Because most current therapeutics target what may be a more differentiated cell type, the success of this proposal could lead to novel strategies for treating prostate cancer. There are very few applications currently funded to identify cancer stem cells in prostate cancer.

National Institute on Alcohol Abuse and Alcoholism

The most serious adverse consequence of prenatal alcohol exposure is fetal alcohol syndrome (FAS), a devastating developmental disorder characterized by craniofacial abnormalities, growth retardation, and nervous system impairments that may include mental retardation. Preliminary data suggests that pharmacological and nutritional interventions may prevent deficits in alcohol-exposed fetuses even when administered following the exposure to alcohol. Recently studies in animal models have shown that choline is capable of preventing deficits due to alcohol exposure in utero. **The fiscal year 2008 President's budget does not provide sufficient funds to proceed with larger scale studies to determine the effectiveness of choline in preventing deficits in humans due to in utero alcohol exposure.**

National Institute of Child Health and Human Development

There will be no expansion of research efforts to translate NICHD-supported basic scientific findings into a new class of antimicrobial agents that could prevent bacterial or viral infections in the gastrointestinal tract, overcoming a major and growing public health problem of bacterial and viral drug resistance. Researchers found that oligosaccharides, non-nutritive components of human milk, inhibit the toxic effects of Escherichia coli and other gastrointestinal pathogens. These pathogens infect thousands of adults, and children, annually, causing extreme discomfort and even death. In the U.S., infections due to C. jejuni, E. coli, and five other food borne pathogens have been estimated to cost $6.5 billion to $34.9 billion annually. The critical advantages of developing these amazing antimicrobial products are that they: a) can prevent both viral and bacterial infections, and b) do not interfere with protein synthesis and bacterial/viral replication. Instead, these compounds prevent the pathogens from binding to intestinal walls, thus overcoming a major and growing public health problem of bacterial and viral drug resistance.

National Institute of Diabetes and Digestive and Kidney Diseases

NIDDK can provide only very limited funding to solicit applications investigating the effect of maternal obesity on mechanisms that could potentially contribute to obesity, diabetes, cancer, cardiovascular or metabolic disease in the offspring.

NIDDK has not been able to initiate an Autoimmune Hepatitis Clinical Research Network which would focus upon elucidating the pathogenesis and developing means of prevention, treatment and control.

National Institute of Neurological Diseases and Stroke

The NINDS developed the Spinal Muscular Atrophy (SMA) Project as a pilot of how to speed the translation of basic science advances to therapies that are ready for clinical testing. The project is implementing a systematic drug development plan via a "virtual pharma organization," which develops and applies the resources for drug development through subcontracts to companies that serve the pharmaceutical industry. **The project is making encouraging progress, enough so to warrant application for a provisional patent on promising compounds that have been developed. Although there are other neurological disorders that might be ripe for a similar targeted therapy development program, NINDS**

would not be able to undertake such an activity under the President's budget.

National Institute on Aging

Specific examples of the potential impact of budget constraints on the momentum of the federally-supported Alzheimer's disease research agenda include:

—**NIA may be unable to maximize data collection efforts or to capitalize on the data being generated through studies under its two recently-released Program Announcements aimed at the discovery, development, and preclinical testing of novel compounds for the prevention and treatment of Alzheimer's disease.**

—**NIA will fund fewer studies under the Alzheimer's disease Neuroimaging Initiative, a public-private partnership that tests whether imaging techniques, other biological markers, and clinical and neuropsychological assessment can be combined to measure with greater sensitivity the progression of mild cognitive impairment (MCI) and early Alzheimer's disease.**

—**Constrained budgets could slow the process of studying and identifying genes through the ongoing Alzheimer's disease Genetics Initiative, which is designed to develop the resources necessary for identifying late-onset Alzheimer's disease risk factor genes, associated environmental factors, and the interactions of genes and the environment. Identification of informative subjects, genetic typing, and data analysis would all be slowed, delaying the identification of genetic and environmental factors that could provide new approaches for the prevention and treatment for Alzheimer's disease.**

National Institute of Allergy and Infectious Diseases

There is an intensified need for the development of a safe, effective and acceptable topically applied chemical and /or biologic barrier to prevent sexually transmitted HIV infection. Topical microbicides hold great promise as a strategy for preventing future HIV infections and AIDS-related complications and are designed to allow women to protect themselves against HIV and other sexually transmitted infections. The NIH supports several research programs and initiatives to help develop and advance candidates into human clinical trials, including the Integrated Preclinical/Clinical Program for HIV Topical Microbicides, Microbicide Innovation Program, and the Microbicide Design and Development Teams. **There are 38 lead microbicide candidates, of which seven are advancing to clinical trials in the next few years, and over 100 proposed candidates in the microbicide development pipeline. Additional funds would allow NIAID to ensure a vibrant pipeline and advance five additional compounds into early clinical studies.**

PREVENTION RESEARCH

The following examples of prevention research should lead us toward the era of personalized medicine, where we will be able to preempt the disease early in its process or even before it starts.

National Institute of Mental Health

NIMH is supporting a prospectively designed research network to predict, characterize, and preemptively treat schizophrenia:

—Schizophrenia is generally diagnosed between ages 18 and 21 when a young person has a psychotic episode that requires hospitalization and intensive treatment.

—However, most people with schizophrenia are ill for at least 18 months before their first psychotic episode—this period is known as the prodromal phase of the illness.

—The goal of this research network will be to determine whether treating schizophrenia during the prodromal phase can prevent psychosis and functional disability. Researchers will identify genomic and imaging biomarkers to define risk and to develop interventions.

National Institute on Alcohol Abuse and Alcoholism

NIAAA is supporting research to identify "trait" biomarkers which are inborn characteristics of increased vulnerability for specific types of alcohol-use disorders including alcohol dependence (alcoholism).

Through the identification of trait biomarkers for the specific subtypes, early preemptive interventions would be feasible in individuals at high risk for future alcohol

dependence, as would interventions in early stages of the disease itself with personalized treatment based on subtype.

National Institute of General Medical Sciences

Part of the difference in how people respond to drugs is due to genetic variations, particularly in the pathways that control drug metabolism. Such variations can render some drugs ineffective in certain individuals or, in other cases, increase the likelihood of dangerous adverse drug reactions. Since 2000, NIGMS has led the Pharmacogenetics Research Network, a trans-NIH effort to elucidate the genetic basis of differences in drug responses and guide the implementation of this knowledge into clinical practice. In several cases, findings by network scientists have already impacted practice, such as by providing genetic tests to support the use (or avoidance) of a given drug. Pharmacogenetics is a leading example of how investments in the Human Genome Project will broadly affect medical treatment, in this case by personalizing drug therapy.

National Eye Institute

The Age-related Eye Disease Study2:

—The Age-Related Eye Disease Study (AREDS), a multi-center study of cataract and age-relate macular degeneration (AMD) originally launched in 1992, demonstrated that high-dose antioxidant supplements (beta-carotene, vitamins C and E, and zinc) can slow the progression of AMD. Additional studies have suggested that the nutritional supplements lutein/zeaxanthin and omega–3 long chain polyunsaturated fatty acids might have benefit in preventing or slowing the progression of AMD and the formation of cataract. Leveraging these findings, the NEI began the Age-Related Eye Disease Study2 (AREDS 2), a multicenter study that will include up to 100 clinical sites.

—It is hoped that data from ARESD2 will improve therapeutic regimens that can prevent or slow the progression of AMD and cataract. It is further hoped that additional study data from AREDS2 will help create prognostic criteria to determine who will likely benefit from these nutrient supplements.

National Human Genome Research Institute

To speed research on the causes of common diseases such as asthma, arthritis, the common cancers, diabetes, and Alzheimer's disease, the Department of Health and Human Services announced in February 2006 two related groundbreaking initiatives in which NHGRI will play a leading role. Using the newly derived HapMap, both of these initiatives will search for the specific DNA variations that are associated with increased risk for common illnesses. Finding the DNA variants that predispose a person to common disease is one of the highest priorities of current biomedical research, since it will enable the identification of new drug targets and the development of personalized medicine.

The Genes, Environment and Health Initiative (GEI) is a trans-NIH research effort to combine comprehensive genetic analysis and environmental technology development to understand the causes of common diseases. GEI will support more than a dozen studies, beginning in fiscal year 2007.

The Genetic Association Information Network (GAIN) is a related public-private partnership between the NIH, the Foundation for the NIH, and private sponsors including Pfizer and Affymetrix. In 2006, GAIN selected six research studies for support: psoriasis, ADHD, schizophrenia, bipolar disorder, major depression and diabetic nephropathy. Results will begin to appear in June 2007.

National Institute of Neurological Diseases and Stroke

Research funded by NINDS has identified specific variants of a gene called phosphodiesterase 4D (PDE4D) that significantly increase the risk of stroke in women aged 15–49. The risk is magnified in women who smoke cigarettes. The study is the first to identify a possible interaction between this gene and an environmental factor in triggering stroke.

This study is part of a larger effort called the Stroke Prevention in Young Women Study2, which is designed to identify genetic and environmental risk factors for ischemic stroke (stroke that results from blockage in artery) in young women. The NINDS-funded investigators are now carrying out a study of risk factors for early-onset stroke in young men to help further clarify the role of the PDE4D gene and characterize the genetic basis for ischemic stroke. This research could help identify those at risk for stroke so that they may modify their behavior and eliminate certain environmental influences (e.g., smoking) to pre-empt the occurrence of a stroke. The research may also help in the development of new types of interventions to prevent stroke in those high risk individuals.

National Institute of Dental and Craniofacial Research

Salivary Diagnostics.—The day is approaching when a tiny computer chip glued to a tooth will allow early, personalized diagnosis and treatment by closely monitoring levels of proteins associated with specific diseases, as well as the medications prescribed to treat them.

—NIDCR support helped develop the current generation of rapid HIV antibody testing that uses intraoral fluid. The OraQuick™ HIV test reportedly has a 99.8 percent accuracy rate, compared to 99.9 percent for a blood test.

—Current grantees recently fabricated the first disposable, low-cost miniaturized diagnostic platform to process small amounts of saliva to detect the levels of DNA sequences of interest. The work is proceeding to ultimately create a fully functional hand-held instrument for salivary diagnostic tests that is about the size of a BlackBerry™.

—In the future, miniaturization of the technology will allow salivary diagnostic chips to be attached to a tooth for continual personalized monitoring of biomarkers for specific diseases.

National Institute of Arthritis and Musculoskeletal and Skin Diseases

The NIAMS places a high-priority on studies to identify risk factors and biomarkers of disease. To this end, the Institute will continue its commitment to a novel public-private partnership to improve prevention of osteoarthritis (OA), or degenerative joint disease. The Osteoarthritis Initiative (OAI) is a long-term effort, developed with support from numerous NIH components, private sector sponsors, and with the participation of the Food and Drug Administration, to create a publicly-available research resource to identify and evaluate biomarkers of OA for use in clinical research. The study has 4,800 participants who are at high risk for knee OA and, as of early fiscal year 2007, clinical data from approximately 2,000 of them were available for research projects. Over the next 5 years, the OAI will provide an unparalleled, state-of-the-art longitudinal database of images and clinical outcome information available to researchers worldwide to facilitate the discovery of biomarkers for development and progression of OA. In this effort, a biomarker would be a physical sign or biological substance that indicates changes in bone or cartilage. Today, 35 million people—13 percent of the U.S. population—are 65 and older, and more than half of them have radiological evidence of OA in at least one joint. By 2030, an estimated 20 percent of Americans—about 70 million people—will have passed their 65th birthday and will be at increased risk for OA.

National Institute of Diabetes and Digestive and Kidney Diseases

Preempting Risk Factors for Type 2 Diabetes in Children:

—Previously considered a disease of adults, type 2 diabetes is now increasingly observed in children, particularly minority youth. Identifying new strategies to preempt risk factors for diabetes is extremely important because recent data estimate that 1 in 14 children in the U.S. between 12 and 19 years of age has pre-diabetes—and many of the children with pre-diabetes have risk factors for cardiovascular disease (CVD).

—In August 2006, the NIDDK launched a multicenter clinical trial, called HEALTHY, which is aimed at preempting risk factors for type 2 diabetes in middle-school children.

—Half of the 42 enrolled schools are receiving the intervention, which consists of: environmental changes to school food service and physical education class activities; behavior change activities; and communications and promotional campaigns.

—Children are being enrolled in the sixth grade and followed for 3 years. Importantly, the schools have large (50 percent or more) minority or under-served populations.

NIH OFFICE OF WOMEN'S HEALTH

Senator SPECTER. Now, we go back to before your time, Dr. Zerhouni. It was about 1991, wasn't it, Senator Harkin, when the woman's branch of NIH was established? Is that correct?

Dr. ZERHOUNI. That's correct. The Office of Women's Health.

Senator SPECTER. There wasn't an Office of Women's Health before this subcommittee picked it up and found the money for it. My wife pointed out to me the difference in heart disease for women, and we took the lead, here in this subcommittee, to establish a

women's unit. So, it's very gratifying to see your statistics this year, that heart disease of women dropped from one-third to one-fourth.

Well, you get my point. I'd like to have it in a concrete form so that we could tell our colleagues, on the budget resolution. As I told you earlier today, Senator Harkin and I are going to be going to the floor and asking for an increase in the budget resolution on NIH. I'm not sure how much it's going to be. We're going to ask for the most we think we can get—that is realistic—that we can get adopted, maybe a little more than that in terms of bargaining. Last year, we increased the budget for the subcommittee by $7 billion. But that's confederate money on the budget resolution. Doesn't turn into real cash until you have an allocation.

I had a disagreement with Senator Byrd, back in 1988, on the allocation for the budget, and I did the unheard of thing for a Senator my age compared to a Senator of his standing, to disagree with a chairman's mark. I got three votes. It was 25 to 3. You may think three votes out of 28's not many, but it's a lot. Senator Byrd told me, at that time, "Someday you'll be chairman of the Appropriations Committee." It didn't seem possible. But now I'm right behind Senator Cochran. With term limits and a change in party, I'm getting pretty close to that, Dr. Zerhouni. If, and when that happens, you won't have to provide all these fancy statistics. But, in the interim, we need them—something really concrete that we can point to—to show our colleagues, as a way of elevating the status of health and how much NIH means to promoting health, our greatest capital asset, and how much it means in reducing costs by preventing disease.

SUSTAINING OUR PRESENT RESEARCH CAPITAL

What do you think, Dr. Zerhouni?

Dr. ZERHOUNI. Let me just give you the three points that I think are essential, in terms of policy, and then also take the opportunity to supplement that answer with specifics for the record.

First and foremost, you asked the question about: What is the optimal way for us to accelerate our research to get to cures as optimally as possible? It's hard to give an answer for any one disease, but I can show you, from my standpoint as a science administrator, what I think the optimal point is in our ability to sustain research.

Let me show you, if you don't mind, a slide, here, of what has happened to NIH success rates. Historically, we've funded about 3 grants in 10 applications. Today, we fund 2 in 10. Our experience, as—myself, as a scientist, when I ran my lab; as a dean for research at a major institution; and now as NIH Director, is that 3 in 10 is the historical percentage where NIH has always sustained its success rate, and where we've gotten the return that we wanted. I'm concerned that 20 percent is too low. I think you will hear, from our scientists, that this is straining the enterprise, and it is also discouraging new generations.

So, if you ask me, "What is the wisdom of science administrators worldwide as to: 'How do you sustain areas of research in cancer,'" or whatever, I think people would say that success rates in the 25- or 30-percent range are a minimum that you need to sustain re-

search over time so that you can, in fact, have a healthy environment.

Now, in this case—and I published these figures—I'm showing you here, in red, the success rate of NIH. If you look, historically, it was around 30 percent, if you follow the line. Then, in about 2002–2003, it dropped. Why did it drop? Not just because we had flat funding. Flat funding did lead to a loss of purchasing power. But here is the real story, Senator. More scientists are needed to study the complexity of the diseases we're dealing with. So, if you look at the curve, the blue curve, this is the number of applications we've received at NIH. You can see there are more scientists now—there are twice as many applications at NIH from twice as many scientists, almost, who want to do research. We can't sustain—not even one-third, not even 30 percent; we are at about 20 percent right now.

So, that's answer number one. If you don't want to lose momentum, that is an objective that you need to look at.

The second is what you said about: What is the greatest impact, and what do we need, to make sure we don't lose? Well, first, as you know, we've made some very tough decisions in not allowing inflationary increases and focusing, as you've helped us this year, on the next generation of scientists. Typically, NIH funds 1,500 new scientists a year who get their first major grant. Last year, we dropped to 1,400. I want to get back to 1,500, because if we don't, 10 years from now you won't have the researchers to implement the cures that will be discovered in the basic research laboratories. So, it's important to realize that we need to sustain that. But that cannot be done without some compromise or some decrease in other areas.

So, we have favored, over the past 2 years, what we call investigator-initiated research—research project grants to individual investigators. At the expense of what? Well, at the expense of clinical trials. If you look at our ability to conduct clinical trials on patients like yourself, you know we want to optimize a protocol for cancer, optimize a protocol for prevention of heart disease—prevention of stroke is another example—we've had to cut these programs, because they're extremely expensive.

I'll give you an example. Clinical trial costs grow faster than inflation, because it's like healthcare, most of the care in the clinical trial cost is healthcare. So, it grows at 7–8 percent. When you have a flat budget, you lose your ability to study as many patients. So, that's what we're seeing. This is what we're giving up. We're giving up the ability to do clinical trials to enable us to change the science and change the medicine that we do. So, that's the second answer that I think is important here, is that the impact is primarily in our ability to translate from the laboratory to the clinic to the bedside and to the community what we need to do to prevent diseases.

But I will be happy to provide you very specific answers, institute by institute, for the record, Senator.

[The information follows:]

REDUCTION IN SOCIETAL BURDEN & HEALTH CARE COSTS

The following examples illustrate how research funded by NIH institutes lead to reduced societal burden and/or healthcare costs:

National Cancer Institute

Tamoxifen.—A Preventative Agent for Breast Cancer

In 2006, breast cancer is estimated to have affected 214,640 Americans. Since 1978, when Tamoxifen was first approved in the treatment of breast cancer, the National Cancer Institute has pursued further research to exploit the utility of this hormone receptor-blocker as a cancer preventative agent. Several studies by NCI and others, using over 20,000 women, confirm that tamoxifen can be given to prevent Estrogen Receptor-positive (ER-positive) breast cancer, and the preventative benefits continue for many years after the women stop taking the drug. ER-positive breast cancer accounts for about 60 to 70 percent of breast cancers. This equates to approximately 128,000 to 150,000 cases of breast cancer that could be prevented annually. NCI previously conducted the STAR trial (Study of Tamoxifen and Raloxifene), with nearly 20,000 women, that showed the benefit for breast cancer prevention when taking either tamoxifen or raloxifene, and for the women taking raloxifene, a lower occurrence of blood clots or uterine cancer.

Cancer Survivorship.—Reducing the Societal Burden

NCI leads the nation in championing research on the health and quality of life of our growing population of cancer survivors, currently numbering more than 10 million, up from only 3 million in 1971. While the ultimate goal of eliminating cancer continues to be our long term commitment, the capacity to dramatically reduce the societal burden caused by cancer, by increasing survivorship rates, is within our immediate reach. Advances in out ability to detect, treat and support cancer patients have turned this disease into one that is chronic or readily managed for many and curable for increasing numbers.

HPV Vaccine.—Societal Benefits and Cost Savings

An important public health milestone was realized when the FDA approved a vaccine that prevents infection by HPV 16 and HPV 18, the two subtypes of the human papillomavirus responsible for up to 70 percent of cervical cancer cases worldwide. This approval is a watershed moment that highlights the very best of biomedical research: the translation of basic and population science into an intervention that will save lives.

Widespread vaccination has the potential to reduce cervical cancer deaths around the world by as much as two-thirds (about 250,000 women). In addition, the vaccine can reduce the need for medical care, biopsies, and invasive procedures associated with the follow-up from abnormal Pap tests, thus helping to reduce health care costs. This advance also allows NCI to stress the continued importance of cervical cancer screening and provides an opportunity to educate the public about HPV. By monitoring benefits and risks of HPV vaccination, we can optimize the use of HPV vaccines to achieve the greatest health benefit for women.

The National Heart, Lung and Blood Institute

During the past several years, American men and women have benefited greatly from continued reductions in morbidity and mortality due to cardiovascular disease. The following new findings from NHLBI-supported research have improved our ability to treat and prevent a range of cardiovascular conditions:

—The ALLHAT revealed that diuretic drugs are at least as effective as newer, more expensive medications in treating hypertension, a major risk factor for coronary heart disease, stroke, and congestive heart failure.

—The AFFIRM trial established the superiority of a heart-rate control approach to treat atrial fibrillation.

—An emergency-room-based study demonstrated the utility of magnetic resonance imaging in rapidly diagnosing acute myocardial infarction, thereby enabling timely intervention to restore blood flow to the heart muscle.

—The PREVENT trial established the efficacy and safety of long-term, low-dose warfarin therapy to prevent the recurrence of blood clots in patients with a history of deep-vein thrombosis and/or pulmonary embolism.

—A community-based trial found that public access defibrillation performed by trained volunteers increases survival for victims of cardiac arrest.

—The Sudden Cardiac Death in Heart Failure trial reported that an implanted cardiac defibrillator significantly reduces deaths among patients with moderate-to-severe heart failure.

—The Prevention of Events with Angiotensin-Converting Enzyme (ACE) Inhibition trial revealed that heart disease patients who are already receiving state-of-the-art therapy do not benefit from additional treatment with ACE inhibitors.

—The Women's Ischemia Syndrome Evaluation study reported a number of important findings regarding diagnosis and prognosis of chest pain in women.

—The SHOCK trial concluded that treating heart attack patients who develop life-threatening cardiogenic shock with emergency angioplasty or bypass surgery greatly improves the long-term survival.
—The first totally implantable permanent artificial heart—the culmination of many years of research efforts by the NHLBI and others—received FDA approval for implantation in certain patients with severe heart failure.
—The Occluded Artery Trial found that late angioplasty after a heart attack offers no advantage over standard drug therapy.

National Institute of Allergy and Infectious Diseases

Adult male circumcision reduces HIV transmission

The NIAID supported two clinical trials in Uganda and Kenya that found an approximately 50 percent lower risk of heterosexual transmission of HIV among adult men who received a medical circumcision compared to men who were not circumcised. These results were announced in December 2006.

The study results indicate that HIV transmission from women to men could be lowered, though not eradicated, by increased rates of male circumcision.

The impact of increased access to male circumcision would be most pronounced in those areas with low rates of male circumcision and high rates of heterosexually transmitted HIV.

Based on the results of these studies, an international expert consultation, convened by the World Health Organization (WHO) and the UNAIDS Secretariat, recommended that male circumcision now be recognized as an additional important intervention to reduce the risk of heterosexually-acquired HIV infection in men.

Modeling studies suggest that male circumcision in sub-Saharan Africa could prevent 5.7 million new cases of HIV infection and 3 million deaths over 20 years.

Survival benefits of AIDS treatment

The NIAID supported a study to quantify the cumulative survival benefits of AIDS care in the United States. The results were published online in The Journal of Infectious Diseases, in June 2006.

At least 3 million years of life have been saved in the United States as a direct result of care of patients with AIDS.

The study data demonstrate the dramatic impact that advances in anti-retroviral therapy have made on the long-term survival of the most vulnerable HIV-infected persons, those who develop AIDS.

The data also underscore the importance of the global implementation of HIV treatment in resource-limited countries and the potential for huge survival benefits in those countries.

National Institute of Diabetes and Digestive and Kidney Diseases

Reducing the Burden of Chronic Kidney Disease and Kidney Failure

Diabetes is the leading cause of chronic kidney disease and end-stage renal disease. Research has shown tight control of blood glucose levels can dramatically diminish the development of complications of diabetes. With good care, fewer than 10 percent of diabetes patients develop kidney failure.

Kidney disease can be detected earlier by standardized blood tests to estimate kidney function and monitoring of urine protein excretion. NIH research has shown that drugs (ACE inhibitors and ARBs) that better control blood pressure can slow the rate of kidney damage by about 50 percent. As a result of improved treatment, the number of new dialysis patients has stabilized, although troubling racial disparities persist.

The savings to Medicare for each patient who does not progress from chronic kidney disease to end-stage renal disease is estimated to be $250,000 per patient. Overall, estimated Federal savings from recent improvements in preventing kidney disease is approximately $1 billion per year.

National Institute on Deafness and Other Communication Disorders

Over the last three decades, the NIH's support has played a significant and important role in the development of cochlear implant (CI).

NIDCD-supported research demonstrates that the sooner a child with severe to profound hearing loss receives a CI, the greater the benefit showing age")appropriate speech perception and language production within six to nine months after the CI is turned on.

NIDCD-supported scientists have found that the benefits of the cochlear implant far outweigh its costs in children. A cochlear implant costs approximately $60,000 (including the surgery, adjustments, and training). In comparison, the services, spe-

cial education, and adaptation related to his or her deafness will cost more than $1 million if a child is born deaf or becomes deaf before the age of 3.

National Institute on Drug Abuse

Declining cancer deaths, in part due to decreases in cigarette smoking, have resulted from better treatment options for tobacco addiction and from effective prevention efforts—buttressed by NIDA-supported research. For the second year in a row, the CDC reported a decline in deaths due to cancer, a remarkable accomplishment stemming from research-backed treatments and public education campaigns.

—NIDA-supported research revealed nicotine as the main addictive component in tobacco, enabling the development of first-line therapies such as nicotine replacement, complemented by behavioral approaches.

—NIDA-supported education and prevention efforts targeting young people have paid off dramatically in falling rates of teen cigarette smoking, now at the lowest point since 1975, when our Monitoring the Future survey of drug use and attitudes among 8th, 10th, and 12th graders was initiated.

—Since most addiction begins in adolescence and even childhood, these declining smoking rates are likely to lead to continued public health dividends as young cohorts with lower smoking initiation rates age.

National Institute of Child Health and Human Development

Progesterone Injections Reduce Preterm Delivery.—Currently, 12 percent of all births are premature and two percent are "very preterm." Ten percent of the very premature babies will die and 15 percent will survive with major disabilities, such as cerebral palsy, deafness, blindness or mental retardation. The Institute of Medicine estimates that the annual societal economic burden associated with preterm birth in the United States was over $26.2 billion in 2005. The NICHD's dedication to advancing treatments for preterm birth has led to the first successful intervention, which has the potential to reduce the associated societal burdens and healthcare costs. Clinicians know that women who have previously experienced spontaneous premature labor are at greater risk than others to experience it again. Findings from a groundbreaking clinical trial showed that treating women, who had a previous preterm delivery, with 17 alpha-hydroxyprogesterone caproate (17P) reduced, by 34 percent, their risk of another preterm birth. The study—conducted within the NICHD's Maternal-Fetal Medicine Units Network—also showed that infants, who were born prematurely even though their mothers were treated with 17P, had significantly lower rates of severe complications. 17P holds tremendous promise for reducing preterm birth and life-threatening medical complications in infants of high-risk women. The therapy will have even greater public health impact when it is extended to other women who are at high risk of preterm delivery. Building on this significant public health advance, researchers are conducting a study to evaluate progesterone therapy in high risk women with twin or triplet pregnancies.

National Institute of Neurological Diseases and Stroke

One of the first systematic studies of the impact of a publicly funded research program on public health and health care costs evaluated the costs and benefits of all NINDS phase III clinical trials from 1977 to 2000. The total cost of the trials was $335 million. The study, published in The Lancet in April 2006, found that over 10 years, the trials provided economic benefits that exceeded $15 billion and were responsible for 470,000 additional healthy years of life. The benefits of the clinical trials program for the entire period covered by the study were estimated to be more than $50 billion, far greater than the total NINDS budget over that period ($29.5 billion). [Johnston et al., The Lancet, 2006, 367:1319–1327].

National Institute of Nursing Research

Program to Improve Knowledge and Coping Helps Improve Quality of Life for Parents of Premature Infants and Reduces Hospital Costs.—Parents of premature infants often endure high levels of stress, anxiety, and depression. NINR-supported investigators tested the ability of an educational intervention program for parents, implemented early in the Neonatal Intensive Care Unit (NICU), to reduce such psychological distress. In what is believed to be first randomized controlled trial of its kind, researchers found that parents in the program, called Creating Opportunities for Parent Empowerment (COPE), demonstrated improved parenting behaviors and reported decreased stress levels compared to parents in a control group. Infants of parents in the COPE program had a 3.8-day shorter NICU length of stay and a 3.9-day shorter total hospital length of stay than did comparison infants, resulting in decreased hospital costs of about $5,000 per infant.

Transitional Care Improves Outcomes for Elders After Leaving the Hospital.—In a randomized controlled trial, NINR-supported investigators evaluated the effective-

ness of a transitional care program in helping to maintain, after hospital discharge, the health and function of elders with heart failure. Elders received a three-month program managed by Advanced Practice Nurses (APNs) that was designed to assist the patients in managing their discharge planning. The APNs worked with the patients to identify goals, individualize care plans, coordinate care across the different settings from hospital to home, and implement a protocol to manage the multiple health issues of heart failure patients. A follow-up evaluation at one year showed that patients who had received the intervention had a longer time before first hospital readmission, along with fewer total rehospitalizations, hospital days, and deaths than a control group that continued in standard care. Improvements were also noted in patient satisfaction and quality of life. The total health care costs over the year-long study period were lower by almost $3,500 per patient for those in the APN intervention group, when compared to a control group.

Senator SPECTER. Thank you very much, Dr. Zerhouni.

Mr. Chairman, we have, on the floor at the moment, the legislation involving the U.S. attorneys who have been asked to resign. I am ranking on Judiciary, and I'm going to have to excuse myself for a few minutes to go to the floor. We are taking up the bill to change the authority of the Attorney General to replace U.S. attorneys on an indefinite basis, which has caused a lot of controversy. That is being debated right now, and I'm going to have to excuse myself to go down there to take care of other responsibilities. Senator Feinstein is on the floor now, and she was scheduled to speak. I'm scheduled to speak after her. But I will be back as soon as I can.

Thank you.

Dr. ZERHOUNI. Thank you, Senator.

Senator HARKIN. Thank you, Senator Specter.

IMPACT OF AN ADDITIONAL $1.9 BILLION

Dr. Zerhouni, just a couple of follow-up questions before we turn to our next panel.

As I said earlier, NIH has lost about 8 percent of its funding, in real terms, since the end of that doubling period, in 2003, which we saw on the screen also. The advocates from different disease groups have asked Congress to get NIH back on track by appropriating a 6.7-percent increase for the next 3 years. By fiscal year 2010, that would equal the amount NIH would have attained if it had simply received inflationary increases. So, this year, a 6.7-percent increase would equate to about $1.9 billion. Just what do you think you could accomplish with an increase of $1.9 billion? What would be different if we could obtain that $1.9 billion?

Dr. ZERHOUNI. Well, again, I think that is—it is key, from my standpoint, to understand that in flat budgets we have to make tradeoffs, and those tradeoffs tend to affect the ability to sustain scientists. So, the ability for us to stay at inflation translates directly into our ability to sustain the scientific workforce of the United States. For example, NIH supports, directly and indirectly, about 326,000 scientists in the United States. Every year that we fall behind, in terms of inflation, we have to make some difficult choices, which typically impact our ability to sustain scientists, who are really the key to scientific progress. So, the first thing that I think staying even with inflation will do is to allow laboratories the resources they need to recruit and retain the scientists that are needed to address the very complex issues that have come to light, from the scientific standpoint, over the past few years.

I think that the other important aspect of it is that we will recover our ability to conduct clinical trials at the rate that we need to conduct them. As I said, we've had a flat funding of clinical trials since 2003—we have not increased the dollars in clinical trials. But, because inflation in clinical trials is 6–7 percent, our purchasing power in clinical trials is 35 percent less than it was 4 years ago.

So, that would be probably be one of the priority areas that we would like to recover, after recovering what I call the optimal success rate. I don't think it's good to have success rates that are persistently low. I think we need to make sure that the opportunities for new scientists and established scientists are recovered.

So, those are the two things. First, maintaining a viable, vibrant workforce—a scientific talent pool of both established scientists and new scientists, so that the pipeline continues as strong as it has been. Second is to be able to do translation, especially when it comes to putting the bench discoveries to practice.

COMMON FUND

Senator HARKIN. The NIH Reform Act that we passed last year puts a big emphasis on the common fund——

Dr. ZERHOUNI. Yes, sir.

Senator HARKIN [continuing]. Again, to support trans-NIH initiatives that benefit all areas of disease research. A couple-three, things. One, again, can you just spend a couple minutes describing what you hope to attain—accomplish that fund, what are some of the examples of the kind of initiatives that would be funded through this effort. Last, how about initiatives for particular diseases? Some diseases cross many institutes and centers. Could they be funded through the common fund?

Dr. ZERHOUNI. Sir, the common fund is about 1.5 percent of the NIH budget today. It really came from the concept of having—as I said, institutes are extremely good at fulfilling their missions; however, science changes, and often there are areas that fall between the cracks, that you need to sustain, especially when it comes to high-risk, high-impact research. So, we want to sustain our ability, despite tight budget times, to fund innovative ideas and innovative scientists. That is a role that I see for the Common Fund.

Second, emerging areas of science that are not necessarily in the priority of any one institute. A good example is nanotechnology. When I became Director the total investment of NIH in nanotechnology was $50 million. There wasn't an institute that really focused on that. The new institute, the National Institute of Bioimaging and Bioengineering, was just created, and that's their mission, but they were too new, and clearly you needed to make a large advance across the board. That's when we use common fund monies, to sort of launch this area.

Another example is what we call molecular libraries. Scientists told us that they needed to have access to more molecules to see if they could understand better the diseases in their own assays. Well, that was not available to NIH-funded scientists. So, the—no institute really has either the mission or the interest or the scope to fund that. So, we funded it. But what is really important, Sen-

ator, is that the common fund is like a glue fund. In other words, it's the—you know, NIH is like 27 fingers; the common fund is the palm, is the coordination, the strategizing of the future of science, funding areas that wouldn't be funded otherwise. It is really to incubate novel ideas. For example, you could have seen the common fund being used in emerging areas of science, like stem cells, at the beginning, or RNA interference. RNA interference is a new mechanism that was discovered in 1998. The work received the Nobel Prize in 2006. When I became Director of the NIH, I was very keen on finding monies to support that area of research. It was emerging at the time. So, that's the kind of uses that you would want to see for the common fund, uses that are at the frontier of science, serve all institutes, that are not specifically for something that will last forever, but it's just like the kickoff fund, if you will. Five years of funding, 10 years of funding, to get a new area of science started.

Think of the human genome. In 1991—I think you were on the committee at the time——

Senator HARKIN. Chairman.

Dr. ZERHOUNI [continuing]. You were the chairman of the Committee—the then-Director of NIH came to you and asked you, as an exceptional measure, to fund the human genome. The human genome was going to be done at the Department of Energy, because they had an Opportunity Fund. NIH did not have that. So, when I talked to my predecessors, Dr. Varmus, Dr. Wyngaarden at that time, they all said the one thing that is needed at NIH is some sort of a common fund for common purposes that emerge unpredictably that we need to respond to. That could apply to a public health emergency, no doubt about it. But, again, it's a revolving venture fund to make the agency nimble, reactive, not to serve specific interests, but to serve the agency as a whole. I don't know if I'm making myself clear.

Senator HARKIN. Can particular diseases, then, be funded through this, or not?

Dr. ZERHOUNI. I would rather not. I would think that the particular diseases that need to be funded should be funded through the institutes that have the missions——

Senator HARKIN. But some of these——

Dr. ZERHOUNI [continuing]. To serve that.

Senator HARKIN [continuing]. Diseases cross a lot of different institutes. That's the problem.

Dr. ZERHOUNI. So, what we do in that case, when there are diseases that are relevant to the mission of multiple institutes, we have other mechanism, where we encourage institutes to work together. For example, we've had an obesity research plan. It's not funded through the common fund. It's the responsibility of different programs in the institutes, so that what we do there is, we encourage the institutes to work together. For example, the strategic plan for obesity research was published and involves over 19 institutes. The neuroscience blueprint is another example of addressing diseases that need to be served by the institutes whose mission is to serve those diseases in their various dimensions.

Unless it's an area that really requires across-the-board stimulus—remember, no initiative in the common fund stays for more than 5 to 10 years, max. That is the idea of the common fund. It's

not to replace, or a new source of funding for special diseases that don't find a home somewhere else. Very important, I think, to keep that in mind.

PUBLIC ACCESS

Senator HARKIN. I appreciate that.

One last thing, we have to move on to the next panel. It concerns public access to NIH-funded research. You have proposed that NIH-funded researchers should have to submit their final peer-reviewed papers to an NIH database after they're accepted by scientific journals, and that these papers should be made available through the database within 12 months after their publication in the journals. What's the scientific value of increasing public access to this research, as you propose? Why 12 months? Why not 6 months? You've asked Congress to require NIH-funded researchers to adhere to this policy; why do we have to do it? Can't you do that on—you know, can't you simply require that through NIH? Why do we have to do it?

Dr. ZERHOUNI. First of all, I think it's important, in the information age that we're in, to make sure that publicly funded research be available in a database that we can search and connect to all the many other databases that are available to us. It is also important not to damage peer review. But it is important to realize that NIH needs to have a—the ability to do that without damaging journals. That's why 12 months, that's why not 6 months. Because most journals will say that 6 month—for 78 percent of journals, 6 months might be okay, but for others that are not published as frequently, it's not—it will damage their ability to sustain themselves. So, I think we need to be more flexible.

What I think we can't be flexible on is the mandatory nature. We've tried voluntary. I have data about how this is working. I mean, you can see here, for example, that the publications that are being submitted represent less than 10–15 percent—the compliance is the red number, the red bar—the compliance is not as high as it should be. I think we should—we need to make this a condition of Federal grant funding, and that's why we need you to express the wish of Congress to do that, as easily as we can.

So, my position is, a mandatory policy seems to be the one that will be necessary for us to achieve our goals. We've tried voluntary. It doesn't seem to be working as well. I think we need to be flexible on the time. I don't think that we should force a date certain, because it would harm some journals and not others.

Senator HARKIN. That's really all the questions I have, Dr. Zerhouni. Is there any last thing that we didn't bring up that you'd want to get out before I——

Dr. ZERHOUNI. Again, I think that what I'd like to say is how appreciative of you and Senator Specter and the rest of the subcommittee I am. I think that it is key that we continue the momentum.

I have been in—I wanted to give you a perspective about international competition. I just came back from Europe. They have decided to focus on life sciences, and accelerate their investment in life sciences. They've just created a new NIH-like institution in Europe, $57 billion of funding in 5 years. I've been to China; there's

a tripling of the research budget. I've been to India; and there is also an increase in research. There are strong attempts to re-recruit back from the United States. I think we definitely need to understand the strategic importance of NIH. I think you do, but I just want to be on the record to say that nothing is more important than sustaining our investment in science and medical research.

Thank you.

Senator HARKIN. Well, Dr. Zerhouni, thank you very much for your leadership, and also, again, I want to thank you for your statement concerning embryonic stem cells. Hopefully, we're going to move ahead on that, this year, put it behind us, and get about funding this much-needed area of research in our society. So, I thank you for your statement today.

Well, Dr. Zerhouni, now, we're going to move to our next panel. Respectful of your time, if you'd like to stay, and maybe there might be some questions we might have afterward, but I——

Dr. ZERHOUNI. I'd be happy to stay.

Senator HARKIN [continuing]. It's not part of the deal, so if you can stay, we'd appreciate it; if not, then that's fine.

Dr. ZERHOUNI. Thank you, Mr. Chairman. I'll be happy to stay.

Senator HARKIN. Well, I appreciate that very much, Dr. Zerhouni.

Let's bring our next panel up: Dr. Iverson, Dr. Brugge, Dr. Siliciano, and Dr. Strittmatter.

Again, for all of you, welcome to the subcommittee. All of your statements will be made a part of the record in their entirety. I'd ask, if you could sum it up in 5 minutes, your major point, I'd appreciate that. We can elucidate more of it in our questions-and-answer period.

So, I'll go in the order in which I called you. Dr. Brent Iverson, distinguished teaching professor of organic chemistry and biochemistry at the University of Texas at Austin, received his bachelor's of science degree from Stanford and his Ph.D. from the California Institute of Technology.

Dr. Iverson, welcome to the committee, and please proceed.

STATEMENT OF BRENT IVERSON, Ph.D., UNIVERSITY DISTINGUISHED TEACHING PROFESSOR OF ORGANIC CHEMISTRY AND BIOCHEMISTRY, THE UNIVERSITY OF TEXAS AT AUSTIN, AUSTIN, TEXAS

Dr. IVERSON. Thank you, Mr. Harkin.

I am here representing NIH-funded scientists at research universities. I was an undergraduate business major at Stanford until I worked in Professor Jim Coleman's laboratory in chemistry research. It was an NIH-funded research laboratory. My undergraduate research experience charted the course that directly led to my scientific career.

My research spans the interface of organic chemistry and molecular biology on the basic science and of the biomedical research spectrum. I am an inventor on 20 patents, many of which are being used by companies right now.

I would like to make three points concerning the importance of growing the NIH budget.

The first point concerns being able to take full advantage of what the doubling allowed us to initiate. In my own lab, the increased

funding provided by the doubling allowed my collaborators and I to develop a powerful new method we call APEx that allows us to enhance the activity of antibodies. Antibodies are the hottest segment of the pharmaceutical industry today, with over 20 now approved, such as Avastin and Herceptin, for treating colon and breast cancer, and Remicade and Humira for treating rheumatoid arthritis and Crohn's disease.

Antibody drugs are so-called targeted therapies because they're capable of seeking out and attacking only their intended disease targets, with remarkable precision; sort of the smart-bomb approach for drugs. The result is a much more concentrated therapy, one that limits many of the serious side effects of traditional approaches.

Our APEx allows us to make existing antibodies more powerful by a factor of 10 or 100 or more. For example, we started with an antibody against anthrax that could delay, but not prevent death, in animals exposed to live anthrax spores. After making the original anthrax antibody about 20 times more potent, our engineered antibody prevented illness and cured animals treated with the same lethal dose of live anthrax spores. That antibody is being pursued commercially by Elusys, Incorporated, of New Jersey, and will hopefully become a stockpiled countermeasure that should be effective past the point at which Cipro alone works.

With APEx, we are starting—we are ready to start working on engineered antibodies that attack a variety of diseases, such as allergies, inflammatory diseases, and cancer. I believe there are many, many researchers like me poised to make a difference with all the tools now in place, but limited by a flat budget. This is not the time to pull back.

My second point concerns basic science breakthroughs. Flat funding, as we have now, has the effect of making grant funding decisions overly conservative. Let me bottom-line it for you. There is currently too little support for innovative, risk-taking, basic research without new money, because the money we are given largely goes to fund the many worthy older ideas. Less than 10 percent of the grants in my research area receive money each round of consideration. Less than 10 percent. There is simply not enough money left over for new ideas that are not yet proven.

In other words, there is not enough money right now for new ideas that could establish new paradigms or provide new opportunities for new therapies, exactly the kind of basic science research that cannot be done in the commercial sector.

For example, I want to draw your attention to the green panel in our report. This is a molecule from my lab that binds to DNA in an entirely new way. It was discovered in the context of an exploratory project designed to move in an entirely different direction, yet it could someday form the basis for a therapy of the target's DNA directly as a point of interaction.

Conservative funding decisions mean there is also not enough money to fund those scientists who have not yet had the opportunity to prove themselves; namely, new faculty members. Further, our current graduate students are being dissuaded from an academic research career by the difficulty young faculty are having in receiving funding right now.

I would like to finish by describing my concerns about science education. I hope all of you understand that the product of NIH funding is not only the research itself, but, additionally, the training of students. For the U.S. pharmaceutical and biotech industries, NIH is, by far, the most important sponsor of projects that result in scientist training. Talk about strategic economic leveraging.

I generally accept three to four new Ph.D. students in my laboratory every year. With the significantly reduced chance of getting a grant funded, I am forced to take proportionately fewer graduate students. In fact, I am not accepting a single new graduate student this year in my antibody engineering laboratory.

Tight funding impacts undergraduate research opportunities, as well. I have had over 100 undergraduates work in my lab. Across our campus, around 1,000 undergraduates will take part in cutting-edge scientific research, many in state-of-the-art labs with NIH funding. Fewer research grants means fewer opportunities for undergraduate researchers.

PREPARED STATEMENT

Together, I view this as a very ominous combination. Not enough money to take advantage of recent advances, a conservative research environment that discourages risk-taking, and not enough support for state-of-the-art science education. I am convinced that a lack of new money today will have a crippling effect on our global competitiveness, and will limit medical breakthroughs for decades.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF DR. BRENT IVERSON

My name is Dr. Brent Iverson. I am a Distinguished Teaching Professor and the Raymer Professor of Chemistry and Biochemistry at the University of Texas at Austin. I am here representing NIH funded scientists at research universities, both public and private. I was an undergraduate business major at Stanford University until I worked in Professor Jim Collman's chemistry research laboratory. My undergraduate research experience in that NIH-funded lab charted the course that directly led to my scientific career.

Today, I want to tell you about NIH funding from my individual perspective, to help put a face on the budget numbers. My research spans the interface of organic chemistry and molecular biology, on the basic science end of the medical research spectrum. I have well over 100 publications, many in the most prestigious scientific journals. I hold 20 current or pending patents, most of which are licensed and are being used by companies across the country.

I would like to make three points concerning the importance of growing the NIH budget. The first point concerns being able to take full advantage of what the budget doubling allowed us to start. In my own lab, the increased funding provided by the doubling allowed the development of a powerful new method we call APEx that allows us to engineer better antibodies.

Antibodies are the hottest segment of the pharmaceutical industry today, with over 20 now approved for the treatment of diseases such as cancer (ex. Avastin and Herceptin, for treating colon and breast cancer, respectively) and rheumatoid arthritis (ex. Humira). Antibodies are even being pursued as a new approach to treating infectious diseases. Antibody drugs represent the new generation of so-called targeted therapies, because they are capable of seeking out and attacking only their intended disease targets with remarkable precision. The result is a much more concentrated therapy, one that avoids many of the serious side-effects of more traditional approaches such as the standard chemotherapeutic agents used to fight cancer.

Our APEx method allows us to take existing antibodies and make them more powerful by factors of 10 or even 100 or more. This can often make the difference

between an effective or ineffective antibody treatment. For example, we started with an antibody against anthrax that could delay but not prevent death in animals exposed to live anthrax spores. After making the original anthrax antibody about 20 times better, our engineered antibody prevented illness and even cured animals treated with the same dose of live anthrax spores. That antibody is being pursued commercially and may soon become a stockpiled countermeasure.

With APEx developed, we need continued strong funding to take full advantage of it. We are ready to start working on engineered antibodies that attack a variety of disorders such as allergies, inflammatory diseases, and cancer. I am very worried that in the current funding climate, our ability to pursue these diseases is going to be severely limited. You can only imagine my frustration at working so hard to develop the means of making a difference, then having limited support to apply it broadly.

I would like to make a second important point, this one concerning basic science breakthroughs. Tight funding as we currently have now has the effect of making grant funding decisions overly conservative. I have been on many NIH funding panels and have seen this phenomenon in action. Right now, only about 10 percent of the grants in my research area receive money, so the panels must choose the "can't miss, sure things" that represent the obvious next steps of research. It is not that the panels are overly conservative, it is just that no panel can reject these proposals because they will almost certainly lead to advances based on the strong scientific foundation upon which they are built. But what about new ideas that are not proven yet? In other words, the ideas that come out of nowhere, establish new paradigms and change the way we think. With such a limited number of grants supported, there is no money in the system for us to work on more speculative projects, ones closer to the leading edge of knowledge. There is also not enough money to fund those scientists who have not yet had the opportunity to generate extensive preliminary results, namely new faculty members.

Scientific breakthroughs rarely come from a research effort aimed at the "can't miss obvious next step". In my experience, our breakthroughs have come when we least expected it while we were exploring beyond the boundary of what we understood well. For example, I want to draw your attention to the cover of the brochure you have been given today. There is an outline of a complicated molecule in the green panel. It is actually a molecule from my laboratory that binds to a large, specific sequence of DNA using an entirely new type of interaction we have named threading polyintercalation. Our molecule is the first reported to bind to the DNA double helix with a topology that can be described as being similar to how a snake might climb a ladder.

This new approach came from a highly speculative project in my lab intended to make an artificial protein, but once we started analyzing the behavior of our molecules, we realized that what we were doing was also applicable to targeting DNA. Although not yet ready for commercial application, imagine a new class of drugs of the future that target the DNA sequences of viruses, bacteria, or cancer cells directly. Talk about getting to the heart of the matter!

Without increased funding, our ability to explore boundaries such as these and make startling breakthroughs is going to be severely limited. True breakthroughs that move science in new directions often take years to turn into a practical new therapy and only occur when scientists are given the freedom to take scientific risks. I am deeply concerned that a lack of money today to explore beyond conservative boundaries will have a crippling effect on medical breakthroughs that will be felt for decades.

As a corollary to this, I am also concerned that the current lack of funding support will take a heavy toll on young scientists in two ways. The most direct is that they will not receive enough funding to launch their careers because there is only enough for the established scientists. As a more indirect effect, I am worried that the bleak funding picture will dissuade the best and brightest from even pursuing a career in academic scientific research.

I would like to finish by describing my concern about science education. I hope all of you understand that the product of NIH research funding to University researchers is not only the research itself, but additionally, the training of students. It is a very simple equation. Limited funding for research now means fewer trained scientists for the future and consequently fewer research breakthroughs for years to come. As a result, I am very concerned that our place as the world leader in medical research is not secure.

I generally accept 3–4 new PhD students in my laboratory every year. My former students now work in academics as professors/researchers or in many companies around the country. With a significantly reduced chance of getting a grant funded, I am forced to take proportionately fewer graduate students. In fact, I am not ac-

cepting a single new graduate student this current year in the antibody engineering lab. The bottom line is that limited funding means we are also limiting the number of students being trained, and I believe our country needs more, not fewer, highly trained scientists to maintain a healthy technology-based economy.

Finally, being on the campus of one of the largest undergraduate institutions in the country, I am acutely aware that NIH research funding has a tremendous impact on large numbers of undergraduates. I have had over 100 undergraduates work in my lab. Across our campus, around 1000 undergraduates will take part in state-of-the-art scientific research, most of it in state-of-the-art labs with NIH funding. The positive impact of this is almost incalculable. Most of these individuals will not go on to become scientists like I did, but they will be able to articulate to the rest of society what science is, and what research means for our country. With every study pointing to the frightening inadequacy of scientific education across our population, a rare piece of good news is undergraduate research. We need leaders in all segments of society who understand science and can make appropriate choices as we chart the increasingly technological future of our country and our world. Again, it is a simple equation. Not enough money for the labs means proportionally fewer undergraduate as well as graduate student research opportunities across the country.

As a University researcher in the prime of my career, I need to see enough money in the NIH budget so that I can take full advantage of what the doubling allowed me to create. There needs to be enough money in the system to help provide an environment that allows risk taking, thus making scientific breakthroughs more likely and allowing young scientists the opportunity to launch their careers. We also need budget growth to continue the essential scientific training of students ranging from undergraduates to PhD's. All of this is essential if the United States is to remain the world leader in both academic and commercial medical research.

Senator HARKIN. Dr. Iverson, thank you very much for that statement.

Now we turn to Dr. Joan. I hope I pronounce that right—Brugge?

Dr. BRUGGE. Perfect.

Senator HARKIN. The chair of the Department of Cell Biology at Harvard Medical School. She received her B.A. in biology from Northwestern, and her Ph.D. in virology from Baylor College of Medicine.

Dr. Brugge, please proceed.

STATEMENT OF JOAN S. BRUGGE, Ph.D., CHAIR, DEPARTMENT OF CELL BIOLOGY, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS

Dr. BRUGGE. So, first I'd like to thank Chairman Harkin and ranking member Specter and the members of the subcommittee for this opportunity to tell you about some of the real remarkable advances in biomedical research that have been made possible by your strong support for NIH.

I also hope to convey, as well, my personal excitement for the incredible potential that's still to be realized in my field of cancer research. Unfortunately, this enthusiasm is dampened by my profound concerns that the past 4 years of flat funding has significantly compromised our ability to fully realize this potential.

When I was a sophomore math major at Northwestern University, my sister was diagnosed with a malignant brain tumor. This event, and her subsequent death, redirected me towards a career in cancer research. Most of my career has been spent in universities and medical schools, but, before becoming a professor and then chair at Harvard, I served as the founding scientific director of a biotech company in Boston, and that—the industry experience has significantly shaped my understanding of the critical issues that are involved in translating basic discoveries into clinical therapies for patients.

So, as you're probably aware, in the early 1970s, when I entered cancer research, it was actually a very heady time for science. Many of us expected, on the basis of the success of the polio vaccine and the congressionally mandated war on cancer, that we would very soon have a cure for this horrible disease, but we very rapidly learned that cancer is not just caused by a single agent, and it's not just a single disease, as Mr.—or Senator Specter pointed out earlier. We now know that there are hundreds of different forms of cancer. In fact, each tumor from an individual patient contains a unique set of genetic changes. So, this unexpected complexity, which is really unique to cancer, presented a huge challenge in the development of effective treatments.

So, actually, over the last decade there has been an enormously rapid pace of discoveries on the causes of cancer, but it's really not until recently that I have felt real confidence that the year—the congressional investment in cancer research was going to pay off much more directly to patients.

So, at this time, our fundamental understanding of the causes of this disease, and the molecular underpinnings, have led to substantially new and revolutionary new approaches to treating cancer. So, as you're probably aware, most cancer therapies that are used today are—very nonspecifically target any kind of proliferating cell. So, that's why there are significant toxicities to blood cells and immune cells, to your hair, digestive system. But the recently developed cancer therapies are aimed very specifically at what we now understand to be the very—the unique vulnerabilities of tumors, the so-called Achilles' heel of tumor cells. This is leading to much more effective and less toxic therapies.

You're probably familiar with some of the many examples of effective drug treatments that are targeting these specific subsets of tumors with specific molecular defects. These successes are actually providing a blueprint for application to many more types of cancer.

So, I think what we now foresee that is in the near future, there—we'll have customized therapies for cancer, that will be based on the specific molecular diagnosis of a tumor. So, this is already being done in breast cancer, where each tumor tissue is evaluated for specific markers that will predict whether a specific drug will work or the specific drug will not work. Results are really dramatic, so these drugs are adding years to the lives of patients—and the most aggressive forms of blood cancer—sorry—breast cancer. So, it's an example of the precision medicine that Dr. Zerhouni introduced.

So, these successes are really just the tip of the iceberg. Underneath the surfaces, there's a real foundation for much more rapid pace of breakthroughs in cancer detection and treatment based on the research investment in the past.

So, this, then, brings me to my profound concerns regarding the state of NIH funding today. Four years of flat funding have had a very significant impact on the trajectory of cancer research. We are losing momentum and the dedicated careers that were fueled by the previous investments. We're damaging the research capacity, and this will certainly delay relief from the cancer burden.

So, you've seen the statistics indicating a 20-percent success rate of grant applications. Let me just give you appreciation for what

those mean—those numbers mean to the team of scientists in the research labs.

While the reported success rate is 20 percent, this number actually represents the success of either first, second, or third submission of a grant, or the eventual success. So, what—the actual first rate of—the success rate on first submissions is actually half of that, around 10 or 12 percent. So, basically, 90 percent of the scientists that apply for grants are not receiving them the first time around. So, what does that mean? That means there's at least a lapse in funding, and perhaps the loss of the grant. So, what happens when a lab director fails to get a grant? The—a lapse in funding forces the lab to cut back, they have to let staff go, and now your efforts are redirected on alternate funding and resubmission of the grant, instead of moving forward. So, this not only forestalls progress, but it also creates an atmosphere of insecurity and anxiety, and that actually precludes conduct of a creative, innovative exploration.

Once the scientist does secure funding after this lapse, this requires retrenching and retraining, and—basically, a loss of continuity is probably the most serious problems for a scientist.

Scientists at all levels are being affected, not just at the higher—not just at the lower echelons, but even at Harvard. There's two to four investigators in every department that I surveyed, that has had a significant lapse or loss of grants, that were rated as outstanding by the peer-review group.

The other thing I think it's important to understand is that even if one is successful in getting a grant over one of these three submissions, each grant is getting cut between 20 to 30 percent. So, at NCI in the last year, there was a cut of 24 to 29 percent. So, for instance, a grant that's $200,000 will now get $140,000. That will barely cover the salary of the principal investigator. So, we're now faced with funding labs at levels that are 7—at levels that we have 7 to 10 years ago, just—with—and that's not—and so, we have to deal with inflation at the same time, a 30-percent increase in mandated stipends, and also the much higher cost of new technologies for state-of-the-art research. So, as a result, every grant is severely underfunded and—for achieving the approved goals—and scientists are starving.

As Brent mentioned, the frustration and anxiety of lab directors is not get—is not going unnoticed by trainees. Young scientists are looking for other venues to exercise their talents where their long investment and training won't be jeopardized by the lottery, even at the highest—even for the most outstanding grants. This has profound implications for science of the future, since we won't be able to fill in the gaps of that lost generation.

Then, last, I'd just like to make the point that we really can't afford to stand still, because the demographics are against us. As you're fully aware, in 2030 there will be twice as many Americans over 65 compared to the number today. So, given that there's a 10-times higher incidence of cancer in individuals over 65, there's going to be a virtual tsunami of cancer. This is staggering not only with respect to the personal suffering, but also the cost consequences of the cancer burden on our economy.

So, I feel that investment now could have profound savings later. According to one report, a 1-percent decrease in cancer mortality is reported to be worth $500 billion to our economy.

So, as Geoff Wahl, who's president of American Association of Cancer Research, has pointed out, unlike a real tsunami, which we have no time to prepare for, we are well aware of the impending crisis, and congressional investment in research has positioned us to make much more rapid progress in translating basic discoveries into the diagnosis, treatment, and eventually prevention of cancer. We really owe it to the public to capitalize on these investments.

I'd just like to finish, then, by making the point that it's through your foresight, and those of other members of the committee, that the public has generously provided a start towards eradicating one of the scourges of human health. But now, just as these new therapies, based on our molecular and cellular understanding of cancer, is emerging, the opportunity to expand them to other types of cancer, to build on them, and to provide for a future of more discoveries, has idled. Dr. Neiderhuber shared with me some slides that he just presented to his Board of Scientific Advisors, and there's this long list—long set of—or numerous slides showing missed opportunities he's unable to fund. This included a list of very important projects, resource development, and clinical trials that were canceled because of this cutback. This is very distressing. These cutbacks are going to delay benefit to the public.

PREPARED STATEMENT

So, we can't retreat now that the—our infrastructure is in place, and we're really mobilized to launch a full attack on this disease. So, for the sake of the American people, please find a political route to keep progress against cancer at a sustainable pace. The research findings are clear, there is a path to major advances. Help us get these advances to the public and fulfill the promises of the best in scientific research.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF DR. JOAN S. BRUGGE

First, let me thank Chairman Harkin, ranking member Specter, and members of the committee for this opportunity to report to you some remarkable advances that have occurred in biomedical research because of your strong support for NIH. I hope that I can convey as well my personal excitement for the incredible potential still to be realized in my own field of cancer research. Unfortunately, this enthusiasm is dampened by profound concerns that the four years of flat funding has compromised significantly our ability to fully realize this potential.

When I was a sophomore math major at Northwestern University, my sister was diagnosed with a malignant brain tumor. This event and her subsequent death redirected me towards a career in cancer research. Most of my career has been spent in universities and medical schools. However, for five years before I came to Harvard Medical School, I served as the Scientific Director of a biotechnology company focused on cancer and other diseases. My industry experience significantly shaped my understanding of issues critical to the translation of scientific discoveries into therapies for patients. It taught me among other things, that though the path to treatment can be arduous, today the path between basic discovery and successful drugsalso can be remarkably short.

The early 70's, when I entered cancer research, was a heady time in science. Many of us expected, based in part on the success of the polio vaccine and the Congressionally mandated War on Cancer, that we would soon have a cure for this horrible disease. However, it soon became evident that cancer, unlike polio, is not a sin-

gle disease with a single cause. There are hundreds of different forms and, indeed, tumors from individual cancer patients carry unique sets of genetic changes. This unexpected complexity—unique to cancer—precluded rapid development of a single vaccine or simple cure.

Though we certainly underestimated the complexity of cancer, the Congressional investment in cancer research is now beginning to pay off. We have made enormous progress in understanding the cause of this disease and its molecular underpinnings. This fundamental information has led to revolutionary approaches to treatment, aimed specifically at the unique vulnerabilities of specific tumors; we now know how to target a tumor's genetic or molecular Achilles' heel. In addition, new imaging modalities and biomarkers provide the potential to identify tumors at early stages when treatments are most effective.

Today, I feel a new confidence that we are poised to make rapid progress in developing effective and less toxic treatments for the myriad different cancers. This confidence is based on initial evidence of success. We now have multiple examples of effective treatments that target the molecular alterations of specific subsets of tumors (such as Tarceva for a subset of lung tumors, Gleevec for chronic myelogenous leukemia, and Tykerb, approved just a week ago for treatment of certain breast cancers). These successes provide a blueprint for the development of treatments for many more types of cancer.

Cancer treatment in the future will involve a molecular diagnosis of each tumor, followed by customized therapies. Already this is being done for breast cancer, in which tumor tissues are probed for several markers that predict which tumors will respond to specific drugs (like Tykerb, Herceptin, or estrogen antagonists) and which will not. The results are dramatic, adding years to the lives of many patients with the most aggressive forms of breast cancer, and sparing patients of treatments that offer no promise of efficacy. For the first time, we are seeing a decrease in deaths associated with cancer. The tip of the iceberg is visible, underneath lies the foundation for a rapid pace of breakthroughs in cancer detection and treatment based on the research investment in the past.

We cannot afford to stand still—the demographics are against us. There is an impending increase in cancer due to the baby boomers aging into their cancer-prone years, which has been referred to as an impending tsunami. You are all keenly aware of the ramifications for government of Medicare entitlements associated with this surge in cancer. But unlike a real tsunami, which comes unexpectedly with no time for preparation, we are well aware of this impending crisis. And We know that the Congressional investment in basic and cancer-focused research has positioned the cancer research community to make more rapid progress in translating basic discoveries into the diagnosis, treatment, and eventually, prevention of cancer. We owe it to the public to capitalize on these investments; failure to maintain the pace of advancement towards reducing the suffering of cancer is not an option the American people should support or will support. We are all in this together.

This brings me to my profound concerns regarding the state of NIH funding today. Four years of flat funding have had a devastating impact on the trajectory of cancer research. We are losing the momentum and the dedicated careers that were fueled by the previous federal investments. We are now damaging the research infrastructure, and this will certainly delay relief from the cancer burden.

While you have seen the statistics regarding grant awards presented by Dr. Zerhouni and others at NIH and are aware of the inflationary erosion of our buying power, the mere numbers mask the profound effects on the research community. I would like to give you an appreciation for what these numbers mean to the cancer research community, which is emblematic of the whole research enterprise. While the eventual success rate of grants is 20 percent, this number reflects success of either the first, second, or third submission of a grant. The success rate of the first submissions is now about half of this; thus the vast majority of scientists are subjected to a lapse in funding and the negative consequences of this. Not only can a lapse in funding force labs to cut back, let staff go, and redirect efforts to finding alternative funding and resubmission, it creates an environment of insecurity and anxiety that is anathema to the conduct of creative, innovative exploration. Recovery after a 6–12 month funding gap requires retrenching and retraining of new staff. Many leads will never be followed up. Loss of continuity is one of the most serious problems for a scientist. For new investigators, repeated failure to launch their research program is also demoralizing, and discourages taking original and risky paths.

Researchers at all levels are affected—those beginning their careers and senior investigators with long and sustained track records of major discoveries. For example, multiple colleagues at Harvard Medical School who are leaders in their field with outstanding accomplishments, are suffering lapses in funding or losing grants that

received priority scores in the 10–20 percentile range. Peer review is too imprecise to distinguish differences in the quality of the grants in this tight range.

Second, in order for the success rate of grants to hit the mandated target number of grants, NIH has resorted to cutting grant size dramatically—at NCI, 24–29 percent (2006). Aggravating this situation are reductions in buying power due to inflation and the 30 percent increase in mandated stipends for graduate students and postdoctoral fellows over the past seven years (an increase that we applaud). Lab directors are faced with carrying their labs at funding levels equivalent to those 7–10 year years ago, at a time when there is a significant increase in cost of the new technologies required for state-of-the-art research. As a result, almost every grant is severely under-funded for achieving the approved goals, and scientists are starving for resources.

The frustration and anxiety of lab directors is not going unnoticed by trainees, and many young scientists are looking for other venues to exercise their talents, ones where their long training investment will not be jeopardized by this lottery in NIH grant review. This has major implications for the science of tomorrow, since we will not be able to fill in the gaps of this lost generation.

I would like to reiterate the long-term implications of the current research budget shortfall on the economy. Cancer incidence for those 65 and older is 10 times greater than for those under 65, and the death rate is 16 times higher. By 2030, 20 percent of the U.S. population will be over age 65 compared with 12 percent in 2004. The cost consequences of this tsunami of baby boomers hitting their cancer-prone years could devastate our economy.

A one percent decrease in cancer mortality is reported to be worth $500 billion to our economy according to an NCI report. Getting these potential new therapies I have outlined to patients will take a significant new investment in translational and clinical research, the cost of which can dwarf the cost of basic research. But without the most promising basic discoveries, we will not be able to improve early stage therapies and more and more translational and clinical endeavors will result in dead ends. We can't be shortsighted.

We recognize the challenges each member of Congress faces in balancing worthy priorities, but I can assure you that from a scientific perspective there is justification for fully supporting basic, translational, and clinical pursuits. Basic science now more than ever fuels the success of effective disease diagnosis, treatment, and prevention in the future.

Through the foresight of the members of this committee and others, the public has generously provided a start toward eradicating one of the scourges of human health. We are in fact in a better place to detect, treat, and potentially, prevent cancer. But just as new therapies based on our cellular and molecular understanding are emerging from our labs, the opportunity to expand them to other types of cancer, to build on them, and to provide for a future of more discoveries has idled. We can't retreat now that the infrastructure is in place and we are mobilized to launch a full force attack on a disease that we now understand. For the sake of the American people, please find a political route to keep progress against cancer at a sustainable pace. The research findings are clear. There is a path to major advances in cancer detection, diagnosis, therapy, and prevention. Help us get those advances to the public and fulfill the promises of the best in scientific research.

Thank you for your time,

Senator HARKIN. Thank you, Dr. Brugge.

I now will turn to Dr. Robert Siliciano, professor of medicine and molecular biology and genetics at the Johns Hopkins University School of Medicine. He received his A.B. degree in chemistry from Princeton, his M.D. and Ph.D. from the Johns Hopkins University School of Medicine.

Dr. Siliciano, welcome, and please proceed.

STATEMENT OF ROBERT SILICIANO, M.D., Ph.D., PROFESSOR OF MEDICINE AND PRINCIPAL INVESTIGATOR, HOWARD HUGHES MEDICAL INSTITUTE, JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, BALTIMORE, MARYLAND

Dr. SILICIANO. Mr. Chairman, thank you for inviting me to testify at this important hearing.

Let me begin by commending you and Senator Specter for your foresight and efforts to double the NIH budget between 1998 and

2003. As Dr. Zerhouni pointed out, we are on the cusp of a dramatic transformation in healthcare, which is the direct result of the Nation's investment in health science. I'm pleased to share with you my own experiences about this transformation and the vital role of funding basic research.

When AIDS first appeared, in 1981, we had no idea what we were dealing with. Between 1981 and the present time, scientists have identified the virus responsible, deciphered its generic code, elucidated its lifestyle, developed a blood test, licensed 22 antiviral drugs, and learned a great deal about human immunology. A uniformly fatal disease has been transformed into one that can now be managed effectively with antiretroviral drugs. A recent study suggests that at least 3 million years of life have been saved in the United States alone as a result of these treatments.

These remarkable advances have come directly from basic science research. Many of the big advances came in the last decade. Many were funded by the NIH. The doubling in funding was central to much of that work. Yet we do not have a vaccine or a cure, and we're now struggling to cope with an epidemic of drug-resistant HIV.

My laboratory, and Tony Fauci's lab at the NIH, have discovered how HIV hides in the body and escapes from the drugs that are being used to combat the infection. We've found that HIV can persist indefinitely in a latent state in long-lived cells of the immune system. In these cells, the HIV genome, is embedded into the host-cell DNA. As a result, the infection can never be cured by antiretroviral therapy alone. This discovery has changed the overall treatment paradigm from a hit-early-hit-hard approach aimed at eradication to a more conservative approach aimed at maintaining lifelong control of viral replication.

In addition to serving as a barrier to cure, this latent reservoir, as we call it, can also store drug-resistant HIV, so that if a patient develops resistance, they will always have that resistance.

Right now, drug resistance is the dominant problem in treating HIV. At our clinic in Baltimore, half of the 3,000 patients have multidrug-resistant HIV, and 10 percent of the new infections are with drug-resistant HIV. In developing countries, the problem of resistance is likely to become even more serious.

Now, many laboratories would like to pursue studies on how to eliminate this latent reservoir and how to control drug-resistant HIV, but, due to flat NIH budgets, research efforts are being scaled back. In my own lab, we're having difficulty taking on new student, and beginning new projects. In the past, I spent about 30 percent of my time applying for grants. Now it's up to 60 percent. Prominent investigators that I know in the field are getting out of research altogether. Fewer scientists want to tackle high-risk problems like this, because they know this kind of research will be difficult to fund.

A colleague of mine has made a major discovery on a unique group of patients who control HIV without medication, has been unable to get funding.

Although we have drugs that can control viral replication, we don't even know when therapies should be initiated. The definitive study of when therapy should be started may not be funded. Why?

Because of insufficient funds for vaccine and treatment trials due to competition for diminishing NIH dollars.

This is particularly unfortunate, because the return on NIH investment can be fantastic. For example, the discoveries made by AIDS researchers extend well beyond HIV. The discovery of how to evaluate levels of virus in the blood has revolutionized the treatment of patients with hepatitis B and hepatitis C infection, and will eventually be applied to all viral infections, including influenza.

At Johns Hopkins, we've seen a marked decline in the level of research grants awarded. Fewer projects are being funded, and NIH support for ongoing projects is being cut. In 2002, the average funding per grant was approximately $142,000 for the School of Medicine; by 2006, it had dropped to $92,000, a decline of 34.8 percent.

America's young researchers are being hit the hardest. I fear that we may lose a generation of inquisitive, enthusiastic scientists if they conclude that NIH funding is out of reach. According to the NIH, 8 out of 10 grant applications are turned down. This is a recipe for disaster.

The situation extends well beyond healthcare. Federal investment in biomedical research is also critical to U.S. competitiveness.

The United States has long been regarded as the world leader in scientific discovery, thanks, in large measure, to policies that encourage innovation. But today we face serious threats to this preeminence, as Dr. Zerhouni has mentioned. Other nations bring strong educational systems, focused government policy, and low-cost workers. Asia and Europe are committing unprecedented resources to scientific—to science and engineering.

PREPARED STATEMENT

Basic science research is essential to America's ability to meet this challenge. In the United States, funding for basic research has long been a Government function. Why? Because basic research much be sustained for years, and even decades, sometimes with no discernible immediate return on the investment. No other entity, other than Government, can take on this role. Aggressive, stable, and sustained Federal spending on NIH and on biomedical research much be understood and embraced as a critical component to America's competitiveness.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF DR. ROBERT SILICIANO

INTRODUCTION

Mr. Chairman and members of the Committee, thank you very much for inviting me to testify today at this important hearing. I am Robert Siliciano, and I am a member of the Department of Molecular Biology and Genetics at the Johns Hopkins University School of Medicine.

Let me start by commending you, Mr. Chairman and Senator Specter, for your efforts and foresight in doubling the National Institutes of Health (NIH) research budget between 1998 and 2003. Many of the amazing advances in health care treatment today are the result of federal investment in research identifying early indicators and causes of diseases. I am convinced we are on the cusp of a dramatic transformation in health care, which is a direct result of the nation's investments in

health science discovery and cures. My fellow researchers on the panel and I are pleased to be here today to tell you about this transformation.

On behalf of myself and all my colleagues at Johns Hopkins, I would like to recognize the persistence of many on this committee for your ceaseless support of NIH's work. I would also take this opportunity to invite you to visit our campus in Baltimore to see for yourselves the exciting work that my colleagues and I—not to mention our students—engage in every day. You will find no more persuasive argument for the value of investing in research than witnessing innovation firsthand.

NIH SUPPORT FOR MY WORK ON HIV/AIDS

Early in the AIDS epidemic, an AIDS patient could expect to enter hospice care within a few years after the diagnosis. However, significant research developments in the area of "Highly Active Anti-Retroviral Therapy," or HAART—that combination of drugs commonly referred to as the "AIDS cocktail" has lead to increasing the survival rate of those diagnosed with HIV. This therapy involves a variety of drugs that attack the virus at different stages of its life cycle, thus reducing its ability to replicate itself in healthy cells. HAART combines drugs that were developed during some of the first stages of AIDS research. By 1990, monotherapy—treatment using one nucleoside analog—was showing some promise, but debate persisted in the research community as to which of this class of drugs were the most useful. In 1995, studies showed that treatment with simultaneous use of two nucleoside analogs would prove more effective in prolonging life. By 1997, combination therapy had expanded to include protease inhibitors and non-nucleoside reverse transcriptase inhibitors, both classes of drugs that attack HIV as it attempts to insinuate itself into healthy cells.

The result of HAART has been the transformation of AIDS from a disease that meant rapid and certain death to a chronic condition that can now be managed over a patient's lifetime. When widespread use of HAART began in the mid 1990s, U.S. mortality rates immediately plummeted—from nearly 41,000 in 1995 to 17,000 in 1997. HAART even proved effective for patients who had already reached the terminal stages of the disease; many were able to leave hospice care and return to relatively normal lives.

For the more than 40 million people infected with HIV, the best current hope for avoiding the fatal consequences of the infection lies in treatment with HAART. The benefits of HAART in reducing mortality are clear, but major questions remain about how best to use HAART and how to make it available to all who need it.

Our work has shown that current HAART regimens cannot cure the infection in most patients because the virus persists in a very stable latent reservoir in resting memory CD4+ T cells (cells that control the activities of all of the other cells). Because HAART is not curative, treatment of HIV infection is a lifelong challenge. Most infected individuals will ultimately have to depend upon HAART to avoid fatal immunodeficiency. Problems of drug resistance and drug toxicity make this an alarming prospect.

My lab is interested in understanding viral persistence and in applying basic studies of viral dynamics in HIV infection to optimizing antiretroviral therapy. Our work on viral persistence began in 1994, with the idea that the capacity of HIV to establish a state of silent or latent infection at the level of individual cells might provide a mechanism for viral persistence in the face of immune responses and antiretroviral therapy. We hypothesized that HIV might capitalize on an extremely fundamental aspect of the immune system, immunologic memory, to ensure its persistence in the host.

At any given time, most of the lymphocytes in the body are in a resting state. When a lymphocyte encounters a bacterial or viral protein that it is programmed to recognize, it becomes activated and begins to proliferate, generating effector cells that eliminate the invading microorganism. Most of these effector cells die, but some survive and return to a resting state as memory cells. These cells persist indefinitely, allowing effective responses to future challenges with the relevant microorganism.

HIV preferentially infects activated CD4+ T lymphocytes, inserting its genetic information into the genome of the host cells and directing the production of new virus particles in a process that usually leads to the death of the infected cells. However, a small subset of the activated CD4+ T cells that are infected with HIV survive long enough to revert back to a resting memory state. Because the expression of HIV genes depends on host transcription factors induced in activated T cells, viral gene expression is automatically extinguished when these cells return to a quiescent state. The result is a stably integrated but transcriptionally silent form of the HIV genome in a memory T cell, a cell whose function it is to survive for years in a qui-

escent state. Upon subsequent re-exposure to the relevant microorganism, the latently infected cell is reactivated and becomes competent for HIV gene expression and virus production. Over the past several years, we have been able to demonstrate the presence and persistence of latently infected resting memory CD4+ T cells with integrated HIV DNA in infected individuals. The cells are present only at low frequencies, reflecting the fact that most productively infected CD4+ T cells die before they can revert back to a resting memory state. Particularly important is whether this small reservoir of latent virus persists in patients on HAART. In the years following the advent of HAART, which began in the mid-1990s, there was considerable optimism that virus eradication might be possible with prolonged treatment, based on analysis of the rapid decay of plasma virus to undetectable levels following the initiation of HAART.

We have shown, however, that the frequency of latently infected cells does not decrease even in patients on HAART who have had suppression of viremia to undetectable levels for as long as seven years. As a result of this discovery in 1999, the overall approach to the treatment of HIV infection has significantly changed. In particular, it became more conservative. Patients were no longer started on therapy as soon as they were diagnosed. Initiation of therapy was delayed until later stages of disease, since there was no hope of eradication. This work raised the possibility that the virus could persist indefinitely in all patients on HAART, leading many investigators to question the wisdom of beginning aggressive therapy with the goal of eradicating the infection, particularly in light of the substantial long-term toxicities of HAART regimens.

Several additional findings add to the seriousness of the problem presented by the latent reservoir. We have shown that this reservoir is a permanent archive for drug-resistant viruses that are generated by inadequate treatment. Once drug-resistant viruses have entered the reservoir, they persist there indefinitely, permanently restricting the patient's therapeutic options. The problem of stored drug-resistance mutations is particularly severe in the case of perinatally infected children, who face a lifetime of treatment.

In 2000, we demonstrated the presence and persistence of this latent reservoir in these children. In addition, we have demonstrated that latency operates at the transcriptional level. Latently infected cells carry integrated HIV DNA but contain little translatable HIV RNA. Unfortunately, the last hope for detecting and targeting latently infected cells was that the cells might be expressing low levels of particular viral proteins, allowing recognition by immune effector mechanisms. It now appears that we may be dealing with a completely silent form of latent infection that will be difficult to target with antiretroviral drugs or HIV-specific immune responses. These findings apply not only to children but to all HIV patients.

In 2001, we became interested in understanding the nature of the low-level virus production that continues in patients on HAART whose plasma virus levels are below the limit of detection of standard assays. We have developed methods for cloning and characterizing the extremely low levels of plasma virus that are present in such patients. We have shown that this virus is generally archival in nature, is devoid of new drug-resistance mutations, and may be derived from the activation of latently infected cells. Most importantly, we do not see evidence for the continued evolution of drug resistance in most patients on suppressive HAART regimens. This provides a counterpoint to our disheartening findings on the stability of the latent reservoir. Although current HAART regimens cannot produce eradication because of the extraordinary stability of the latent reservoir, they can largely halt virus evolution, affording patients the possibility of lifelong suppression of viremia if the problem of drug toxicity can be overcome.

It is important to point out that despite the spectacular advances that have been made in anti-retroviral therapy—at least 3 million years of life have been saved in United States alone—the definitive study that would allow us to determine when exactly treatments should commence may not be funded because of insufficient funds for vaccine and treatment trials. An unfortunate tension exists due to this competition for diminishing NIH dollars.

It is also worth pointing out that the discoveries our community of researchers have made extend well beyond HIV. What we have learned from studies of HIV can be applied to other viruses. For example, we have learned how to measure the amount of virus in the blood. This knowledge, which has provided us with a real-time measure of the amount of viral replication in a patient, along with the importance of utilizing it to treat viruses such as influenza and Hepatitis B and C, has revolutionized the success of these treatments.

In the future, we hope to address several critical questions related to the molecular mechanism of HIV latency and the clinical implications of this form of viral persistence. We are interested in whether it will ever be possible to eliminate this

reservoir. Furthermore, we hope to translate our findings on mechanisms of viral persistence into new approaches for optimizing antiretroviral therapy. The correct choice of a HAART regimen is literally a matter of life and death for many patients, and we feel basic studies of viral persistence can be applied to improving decisions about how and when antiretroviral therapy should be given. Over the years, this research has received nearly $7 million in support from the NIH.

I want to emphasize that many labs would like to pursue the problem of how to eliminate the latent reservoir, but everyone I know has had to scale back research efforts because of flat NIH budgets. In my own lab we are now finding it difficult to take on new staff and begin new projects. Typically, in the past, I would spend about 30 percent of my time applying for grants; now about 60 percent of my time is spent preparing applications. Furthermore, some prominent investigators are getting out of research. Few scientists want to tackle high-risk problems like this because research of this type is more difficult to fund. In fact, a very good colleague of mine has made a major discovery on a unique group of patients who control HIV without medication. He has not been able to get funding even though the potential savings is more than $14,000 annually per patient. Additionally, a mentor of mine, and one of the most respected people in the field, is thinking of getting out of research because he has no funding.

FEDERAL INVESTMENT IN RESEARCH IS A CRITICAL COMPONENT OF OUR NATION'S COMPETITIVENESS

The United States has long been the world leader in scientific discovery, thanks largely to government policies that encourage innovation, improve education, and facilitate the transfer of knowledge from the laboratory to the marketplace. Today we face serious threats to this preeminence. Other nations bring to the table strong educational systems, focused government policies, and low-cost workers.

Basic research is essential to our ability to meet this challenge. William R. Brody, president of The Johns Hopkins University and co-chair of a national committee on competitiveness, puts it this way: "Knowledge drives innovation. Innovation drives productivity. Productivity drives economic growth." Our ability to compete in the global economy depends, first and foremost, on our ability to continue making new discoveries. The more we learn about how things work—the principles of basic biology, chemistry, physics, and mathematics—the more opportunity we have to put that knowledge to work. When we know more, we can use that knowledge to make our world better, to build new businesses, devise new products, and to improve our standard of living.

America's most innovative industries are built on decades of basic research, research that had no discernable practical application at the time it was undertaken. For example, the highly theoretical world of quantum mechanics spawned the semiconductor industry and the information revolution. Johns Hopkins scientists thinking about the principle of physics, called the Doppler effect, used it to invent what became today's Global Positioning System. Two Johns Hopkins biologists shared a Nobel Prize in 1978 for using restriction enzymes to cut DNA into fragments that created today's thriving biotechnology industry, which is based on genetics.

In the United States, funding basic research has long been a governmental function. Why? Because it takes a long time to do it, because there is always a risk that any single project will come to nothing, and because it is difficult to capture an immediate return on investment for an idea that has not yet been developed to the stage of a marketable invention.

Despite a societal consensus that basic research is a government responsibility, U.S. Federal research and development spending, as a percentage of Gross Domestic Product (GDP), peaked 40 years ago in 1965, at just below 2 percent of GDP. In the past 40 years, that percentage has diminished by more than half, to about 0.8 percent of GDP. Overall R&D spending, especially in basic sciences, continues to decline. We must reverse this trend now, by strengthening the Nation's commitment to science related federal agencies and departments.

The investments in biomedical research being made by rising economic powers such as China are increasing. While China lacks a central institution like the NIH to oversee its national investment in biomedical research, its National Science and Technology Plan for 2006–2020 emphasizes a long-range strategy to raise its biomedical research to world-class standards. This is being supported by a pledge to raise R&D spending from 1.3 percent of GDP in 2005 to 2.5 percent by 2020 (Science 9 March, 2007: Vol. 315. no. 5817).

If we look to one promising field of the future—that of nanotech—overall government spending globally grew by 10 percent to $6.4 billion in 2006. According to a report released by Lux Research, the United States came out on top, with $1.78 bil-

lion, followed by Japan and Germany. But China actually ranks second when purchasing power parity is considered. China's funding is the equivalent of $906 million. (UPI 9 March, 2007). In this sector, like so many others, China will compete.

The life sciences research funded by the NIH is a key component of our overall national science agenda. For example, Johns Hopkins University is the nation's leading recipient of federal research grants. In fiscal year 2005, our researchers attracted nearly $1.3 billion in federal R&D funding and $1.4 billion in overall R&D funding, a category in which Johns Hopkins has led all U.S. institutions for 27 consecutive years. This support enables us to improve medical care worldwide, advance human knowledge, and train new generations of innovative researchers.

Investment in research universities like Johns Hopkins yields tangible economic benefits as well. In 2006, Johns Hopkins researchers filed more than 420 U.S. patent applications, received 79 U.S. patents, and licensed 72 technologies for commercial development. Some of these inventions will be commercialized by Maryland companies. Already, there are at least 19 existing Maryland-based start-ups bringing Johns Hopkins technology to market. That is a tremendous amount of knowledge made available to American business and the American public for an incalculable range of benefits.

While the President and Congress have embraced the notion that funding for basic research in the physical sciences is essential to strengthening America's competitive standing in the world, and Johns Hopkins certainly recognizes and appreciates the significant investments included in the fiscal year 2007 Continuing Resolution, we remain concerned that funding for biomedical research has not kept pace with this commitment. Aggressive, stable, and sustained federal spending on the NIH and biomedical research must be understood and embraced as a critical component of America's competitiveness.

JUSTIFICATION OF NIH FUNDING

On January 15, 2007, President Bush signed the National Institutes of Health Reform Act of 2006. While the law calls for a 6 percent increase for fiscal year 2007 and an 8 percent increase for fiscal year 2008, the reality is that this funding commitment has not fully materialized. For fiscal year 2006, the NIH budget was cut in both nominal and real terms. For fiscal year 2007, the NIH received a modest yet important increase of approximately $620 million. We are very grateful that this Congress chose to single out the NIH, along with several other science agencies, to be among the few areas of federal spending to receive increases. We recognize that budgets are tight and we see this as a critical statement of Congress' desire to strengthen and preserve the scientific enterprise in this country. Despite this increase, however, fiscal year 2007 marks the fourth year in a row, when adjusting for inflation, that NIH funding has been cut.

At Johns Hopkins, we have annually led the nation in NIH research dollars and we have seen a marked decline in grants awarded to our School of Medicine. Fewer projects are being funded and NIH support of on-going investigations is being cut. Recent figures suggest that the number of grants and overall funding levels have declined. In fiscal year 2002, the average funding level per grant was $142,210 for the School of Medicine. By fiscal year 2006, the funding level dropped nearly $50,000 per grant to $92,683, a decline of 34.8 percent. Hardest hit are America's young researchers. I fear that we may lose a generation of enthusiastic, inquisitive scientists if they conclude that NIH grants are out of reach.

FLAT FUNDING THREATENS OUR YOUNG INVESTIGATORS

One of the first and earliest victims of declining NIH funding has been the young investigator. You have heard today, and often over the past several years, from Dr. Zerhouni regarding NIH's concern that we are potentially sacrificing an entire generation of young scientists. The Director's concern is real and very serious.

Quite simply, we have to do more to support and encourage our young investigators. Most ideas that turn into Noble Prizes come from investigators before they reach the age of 40. As a country, then, shouldn't we be supporting these scientists when they are in their professional prime? Unfortunately, the statistics tell an entirely different story. In the case of initial R01/R29 awards, between 1970 and 2004, the average age by which an investigator with a Ph.D gains his or her first award has gone from 34.3 years of age to 41.7. In the case of MDs, during this same period, that age has gone from 36.7 years to 43.3 (AAMC 12 July, 2006). With diminished NIH funding, our young scientists are witnessing firsthand the decline in overall success rates for grant applications. In 1998, the first year of the doubling, overall success rates were about 31 percent for grant submissions. For 2007, the success rate is projected to drop to only about 19 percent. Left unaddressed, there

is no question that the current decline in NIH funding places an entire generation of young scientists at risk.

Even at my own institution, where we have many of the best and brightest among the current generation of young scientists, we are seeing many of these men and women unable to gain funding support. Without sustainable and predictable increases in NIH funding, this nation is at risk of losing an entire generation of scientists.

RESEARCH IMPACTS HEALTH CARE COSTS

When advocates for increasing biomedical research funding meet with members of Congress and their staff, they are often asked: "What have we to show for the money that NIH has received in the past?" As we think about this question, it is important to recognize that the pace of biomedical research and science in general is often slow and unpredictable. It may be years before we can point to specific therapies or new medical devices that can trace their origins to recently funded efforts. But the simple answer is: We have a great deal to show!

Here are three powerful examples—there are, of course, many more—of what Johns Hopkins scientists have accomplished in terms of improving healthcare and reducing costs, thanks to NIH support.

Detection of Vision Problems of Diabetics

Diabetes is the leading cause of blindness in adults, with 12,000 to 24,000 new cases each year. Early identification of retina disease is critical to stave off vision loss, especially for the 10 million diabetics who are 60 years or older, most of them on Medicare or Medicaid. Yet more than half of all diabetics fail to get an annual eye exam as recommended by the American Diabetes Association. To address this dilemma, Dr. Ran Zeimer, director of the Ophthalmic Physics Laboratory at the Johns Hopkins Wilmer Eye Institute, came up with a novel solution after more than a decade of research: Why not develop an easy-to-use digital camera that tests for retinopathy when diabetics visit their primary care physicians for check-ups?

Thanks to NIH support, Dr. Zeimer perfected an instrument called the DigiScope. The DigiScope takes images of the retina in just minutes as patients sit in front of an automated camera and look at a series of blinking lights. These images are then transmitted via the Internet to a reading center for expert interpretation. More than 20,000 individuals not under the care of an ophthalmologist have been screened to date in the offices of primary care physicians. Those with vision-threatening disease have been identified and referred to eye specialists. In most cases, diabetics without complications are spared visits to an ophthalmologist, while Medicare and Medicaid are spared an expense.

Advances in Treatment for Sickle Cell Patients.

Thanks to continuous NIH grants extending back to 1982, Drs. George Dover and Samuel Charache of Johns Hopkins spent their careers fighting sickle cell disease—a miserable, inherited illness in which sickle-shaped red blood cells get stuck in narrow channels and block blood flow to tissue and vital organs. Patients with sickle cell disease—72,000 in the United States—suffer frequent bouts of fatigue and shortness of breath, joint and body organ pains that turn excruciating and lead to frequent hospitalizations. The pneumonia-like conditions, chest pains, and fever can be life-threatening. Until fairly recently, early death was the norm, with life expectancy for a sickle cell patient projected to be only 20 to 30 years.

In the 1990s, Drs. Dover, Charache, and their Hopkins research team found that a cancer drug (hydroxyurea) did remarkable things for sickle cell sufferers. A 1995 NIH-supported multi-center study proved that hydroxyurea therapy dramatically reduces the frequency and severity of painful episodes, hospitalizations and transfusions. In a 2003 study, daily doses led to 30 percent fewer hospital days, 58 percent fewer transfusions, and a 40 percent reduction in deaths. Today, hydroxyurea therapy is recommended for adults and adolescents with moderate-to-severe recurrent pain. As a result, the life expectancy for sickle cell patients has doubled.

There have been financial benefits, too. According to another NIH-sponsored study, hydroxyurea therapy saves the U.S. health care system $5,210 per sickle cell patient per year. With 72,000 Americans suffering from sickle cell disease, the potential annual savings is more than $375 million annually.

Faster Diagnoses in Emergency Rooms

With the existing threat of bioterrorism, it is crucial to find ways to swiftly identify patients in hospital emergency rooms who have biochemical pathogens or life-threatening infectious diseases, such as meningitis, sepsis, and bacterial endocarditis (an infection of the inner lining of the heart or heart valves). Current test-

ing methods are time-consuming and usually lead to delays in diagnosing and treating these diseases. The current blood and culture tests for some diseases can take 24 hours or more.

Dr. Richard E. Rothman of the Johns Hopkins Department of Emergency Medicine is working on novel ways to identify quickly multiple blood-borne and pulmonary infectious diseases and bioterrorism pathogens. His patented molecular diagnostic tests involve both exhaled breath and body fluids. Early experiments have shown that these new diagnostic tools can detect 25 common bacterial infections and five categories of bioterrorism agents in fewer than 4 hours. Faster response times are expected as the diagnostic tools are fine-tuned.

CONCLUSION

Thank you for your efforts to strengthen America's biomedical research community. Johns Hopkins stands ready to support you in this important endeavor. I invite you and your staff to visit our campuses, explore our facilities, and meet our researchers who are taking the lead in these vital fields.

Senator HARKIN. Dr. Siliciano, thank you very much. I'll have some questions about the drop in GDP, also.

Now we'll turn to Dr. Stephen Strittmatter, professor of neurology and neurobiology at Yale University School of Medicine. Dr. Strittmatter earned his undergraduate degree from Harvard and his M.D. and Ph.D. degrees at Johns Hopkins.

Dr. Strittmatter?

STATEMENT OF STEPHEN M. STRITTMATTER, M.D., Ph.D., PROFESSOR OF NEUROLOGY AND NEUROBIOLOGY, YALE UNIVERSITY SCHOOL OF MEDICINE, NEW HAVEN, CONNECTICUT

Dr. STRITTMATTER. Chairman Harkin, I thank you for the opportunity to share some of my thoughts on NIH-supported science and the NIH budget.

To be frank, my three decades in clinical neurology and basic neuroscience have convinced me that the recently flat NIH budget is stifling creative high-risk research. On the one hand, the doubling of the NIH budget that was provided by Congress and championed by you and the rest of this subcommittee has laid the foundation for fantastic advances, revolutionizing the care of patients with nervous-system diseases; however, for most types of neurologic and psychiatric diseases, we still face a crucial hurdle: the translation of basic molecular analysis of brain function into effective treatments. To leap over this translational hurdle requires the most creative and risk-taking experiments, including those that may lead to an experimental dead-end before achieving a critical insight towards a new therapy.

Regrettably, the decline of inflation-adjusted NIH spending in recent years has produced a marked chilling effect specifically on this type of research. If that's not reversed, we're going to fail to reap the full benefits of the expansion that occurred from 1998 to 2003 in research in the United States.

My own field in neuroscience relates to nerve-fiber growth and provides one example of how high-risk research can succeed when the environment is appropriate. In humans, single nerve cells extend fine threads, called axons, for very long distances, up to 3 feet. You can imagine, if the cell body were blown up to the size of a baseball, the axon would be the width of a pencil and extend for half a mile. When all these nerve fibers are correctly connected, this provides the wiring of the brain, and the function of the brain is critically dependent on all this being connected correctly.

During the 1990s, molecular insights into the basis of axon guidance advanced very rapidly. We identified dozens of axon guidance molecules and genes that help put the brain together. These molecular insights were fascinating, but they didn't immediately improve human health. So, the next step was to apply this knowledge to settings of neurologic injury, where axonal disconnection occurs. The clearest example of this, one—a field that I work in—is traumatic spinal cord injury. Despite the profound, and the persistent, neurologic deficits that occur after spinal cord injury, such as the inability to move or feel below the level of the injury, nearly all of the nerve cells remain intact. The primary cause of disability is the disconnection of one nerve cell from another, not the loss of cells. Very little axon regrowth occurs after injury, and this is why there's very little recovery in adults.

So, here's the translational problem, the hurdle, to overcome. How do we use basic knowledge about axon growth to restart—during development—how do we use that to restart adult axon growth, repair function, and recover ability of people to live a productive life? It's certainly a problem that I wanted to take on as a neurologist caring for patients while running a basic developmental laboratory. However, without the sort of environment that was created by the budget doubling through the NIH funding, I wouldn't have tackled this problem myself. But when I did take it up, in that time period, we discovered, in my laboratory, a molecule, termed Nogo, that prevents nerve fiber growth. By analyzing the mechanism of action of this Nogo molecule, we identified genetic, and then pharmacologic means to prevent its function; thereby, stimulating nerve fiber growth. Remarkably, therapy with a Nogo receptor antagonist allows rats to walk after spinal cord injury or to recover better paw use after a stroke. Today, a closely related approach using an antibody against Nogo is in clinical trials.

So, I think this illustrates how high-risk research can occur. But I'm convinced that similar challenges in Alzheimer's or in schizophrenia research are not being tackled today, because of the limitations that have occurred in the NIH budget. The reason I say that is that when researchers and peer-review panels are faced with the idea that junior investigators can't be funded at all, or that senior investigators are losing funding, everyone shifts towards what I'd call "safe science." Scientists pursue those experiments that have the highest probability of success in the short term, incremental gains. They shy away from the paradigm-shifting discoveries that will really move science into the clinic, where it will solve the major health problems that we have caring for this country.

Researchers essentially become worriers focused on how to maintain their laboratories, rather than explorers seeking to solve the crucial issues. High-risk, high-payoff studies are what we need most, but they have the most volatile dependence on the NIH funding level.

PREPARED STATEMENT

Of course, Dr. Zerhouni and the NIH have recognized the need for this kind of research, and they've taken steps to achieve it within the confines of the NIH budget. This is certainly important and commendable, but it's not a substitute for the kind of investment

of Federal funds that will encourage creativity and reward risk. Specialized programs or set-asides, by definition, can only affect a small percentage of all the research that's going on. Moreover, creativity cannot be dictated by policy alone. Only a reversal of the inflation-adjusted decline in the NIH budget can reset the community's outlook. By establishing an NIH funding level that, at a minimum, restores recent net losses to inflation and keeps pace with costs in the future, Congress, this committee, can achieve the research environment required to promote the health of all of our citizens.

Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF DR. STEPHEN M. STRITTMATTER

Chairman Harkin, and Members of the committee, I thank you for the opportunity to offer my insights on the NIH budget. To be frank, my three decades in clinical Neurology and basic Neuroscience research at Yale, Harvard and Johns Hopkins have convinced me that the recently flat NIH budget is stifling creative, high-risk research endeavors.

The doubling of the NIH budget provided by Congress, and championed by many of you on this committee, laid the foundation to revolutionize the care of those suffering with nervous system diseases. However, for most types of neurological and psychiatric disease, we still face the crucial hurdle: the translation of basic molecular analysis of brain function and dysfunction into effective treatments. To leap over this translational hurdle requires the most creative and the riskiest experiments, including those that may lead to an experimental dead-end or multiple failures before achieving the one critical insight that will establish a new therapy. Regrettably, the decrease of inflation-adjusted NIH spending in recent years has produced a marked chilling effect on precisely the type of research that is most needed. If this chilling effect is not alleviated, we will fail to reap the full benefits of the research expansion that occurred from 1998–2003—and we will push better treatments farther into the future.

My own field in Neuroscience relates to nerve fiber growth, and provides an example of how high-risk research can succeed in the appropriate environment. In humans, single nerve cells extend fine threads, called axons, for distances as long as a meter. If the cell were magnified to the size of a baseball, the axon would be the width of a pencil and extend for half of a mile. These axons conduct electricity and provide the "wiring" of the brain. There can be no useful brain function unless these fibers are correctly connected, and failure to connect—or reconnect—contributes to many diseases, from strokes, Alzheimer's and Parkinson's to Multiple Sclerosis and Lou Gehrig's disease.

Twenty years ago when I started in this field, little, if anything, was clear about how the cells of the developing brain become connected over long distances. However, molecular insights into the basis of axonal guidance began in the early 1990's and the pace of discovery accelerated rapidly during the NIH budget doubling. Basic studies led to the identification of dozens of axon guidance molecules and genes with defined roles in the developing brain.

These molecular insights were fascinating from the scientific perspective, but did not immediately improve human health. The next step was to apply this knowledge to settings of brain injury where axonal disconnection occurs. The clearest example is traumatic spinal cord injury. Despite the profound and persistent neurological deficits after spinal cord injury, such as the inability to move or feel, nearly all of the neurons that initiate arm and leg movements and provide skin sensation survive injury. The primary cause of disability is the interruption of nerve fibers—not the loss of cells. This, we learned, has important implications for treatment.

Inside the brain and spinal cord, very little axon regrowth occurs after injury, explaining the poor recovery of adults. Here the translational hurdle emerged: how do we use basic knowledge of embryonic fiber growth to restart axonal growth and restore proper function after injury or disease. As a Neurologist caring for patients while directing a brain development laboratory, I was particularly keen to attack this hurdle. Despite my interest, I would not have pursued this goal in 2000 without the risk-taking climate created by the NIH budget doubling.

We discovered the existence of a molecule, termed Nogo, which prevents nerve fiber growth, and mice lacking the gene for Nogo or its partner NogoReceptor exhib-

ited significant axonal regeneration. Moreover, such animals recover substantial walking after spinal cord injury, or improved paw use after stroke. By analyzing the action of the Nogo molecule, we identified methods to prevent its function. Remarkably, therapy with a NogoReceptor antagonist allowed rats to walk after spinal cord injury and those with strokes recovered greater paw use. Today, a closely related approach using an antibody directed against Nogo is in clinical trials.

While this story illustrates past progress in high-risk research, I am convinced that similar challenges are not being tackled today because of the NIH budget situation. When researchers and peer review panels are faced with many junior investigators failing to achieve NIH research support and established investigators losing support, the first change is a retrenchment to "safe" science. Scientists pursue those experiments that have the highest probability of achieving an incremental short-term goal, rather than a chance of generating a paradigm-shifting long-term discovery. Researchers have become "worriers" focused on how to maintain their laboratories and jobs, rather than "explorers" seeking to solve the most crucial translational issues. High-risk, high-payoff studies have the most volatile dependence on NIH funding levels. Nonetheless, we require high-risk endeavors now more than ever to take advantage of basic science and research tools developed during the doubling of the NIH budget.

Dr. Zerhouni and the NIH have recognized the need for high-risk, high-payoff research and have taken steps to foster such work within the confines of restricted NIH budgets. This is important and commendable but it is not a substitute for an investment of federal funds that encourage creativity and reward risk. Specialized programs and set-asides can only affect a small percentage of biomedical research by their very nature. Furthermore, creativity cannot easily be dictated by policy. Only a reversal of the inflation-adjusted decline in the NIH budget can reset the biomedical community's outlook.

Future health care can be dramatically improved if researchers explore the highest risk research areas, allowing researchers to clear the translational hurdle and bring the benefits of expanding basic science to the public. By setting an NIH funding level that, at a minimum, restores recent net loses to inflation and keeps pace with costs in the future, Congress can achieve the research environment required to improve health for all of our citizens. I would be pleased to answer any questions.

Senator HARKIN. Thank you very much, Dr. Strittmatter

Just some general questions for the panel. We've all heard about the drop in the success rates, from 1 in 3 to about 1 in 5 right now. Some institutes are rated even lower. I'm concerned that when you get that low, some scientists, especially the young investigators, will just say, "Why bother?" You've all kind of spoken to that, in one way or the other. But what's the minimum success rate that makes sense? What should we be aiming for? Is there something we should be aiming for? What's the minimum? I just open it up.

Dr. STRITTMATTER. Well, I don't know if there's one minimum. There's not one answer to the question. I think Dr. Zerhouni put forth the notion that, historically, the success rate of grants had been around 30 percent. That's one where the culture of research in the United States is comfortable with the idea that we choose the best grants, we move forward with the best ideas. The problem now is that that funding rate has gone down, so we not only—the feeling that scientists have is not that creativity or risk-taking is rewarding, but that we should shut down. We're going backwards, not forward. So, perhaps reaching back to that historical level, not 100-percent funding, but——

Senator HARKIN. Yeah.

Dr. STRITTMATTER [continuing]. 30-percent success rate in grants, will restore the kind of driving forward of the research, moving science into changing healthcare that we need.

Senator HARKIN. That's——

Dr. STRITTMATTER. That's one answer. I don't know——

Senator HARKIN [continuing]. Sort of, overall. Should there be some areas where it should be higher than 30 percent?

Dr. STRITTMATTER. Well, I think one way to judge that would be whether there's—what you'd really want to know is whether, on the margin, the grants that are funded discover something useful, advance healthcare. If funding levels were at 30 percent, do the worst 1 percent or 2 percent of the grants help the American public? I think you could easily argue that the enormous cost of healthcare—they're so large that looking for cures, or preventive, pre-emptive medicine, has such a huge financial benefit—I think that's what Dr. Zerhouni alluded to with his figure of $44 per person in the United States for all of the NIH budget. You could easily argue that we should be at a higher level, and we would still save immense amounts of money compared to the amount that we spend on healthcare and insurance otherwise. That's one answer.

Dr. IVERSON. If I could answer that specifically—excuse me—I would say that, from my perspective, I think 30 percent is a great number. I would also like to see an allocation for a common fund that can be targeted at particularly exciting opportunities that should not fight each other.

Senator HARKIN. Uh-huh. Anything else?

All right. The other thing—Dr. Siliciano, you pointed out in your statement—you didn't state it, but I read it—and it said that—when was it? In 1965, we peaked at the percent of our GDP that went for—was that all R&D—I guess, just all R&D lumped together? Now it's about eight-tenths of 1 percent.

Dr. SILICIANO. Yes, I believe so.

Senator HARKIN. Then you pointed out that China had just recently committed going from 1.3 percent, where they are now—so, they're even higher than we are as a percent of GDP—to 2.5 percent of GDP by 2020. I'm going to have my staff find out what it would be if we were at 2 percent right now? I just wonder what the figure might be. I didn't see it there, but we can find that out. I just didn't know if you knew it, off the top of your head.

Dr. SILICIANO. I don't—not off the top of my head.

Senator HARKIN. Well, obviously it would, what, at least 2.5 times where we are right now.

The other thing that I—you talked about these—about 30-percent approval rates and what should the right number be, what should we aim for. I still don't know if I got a good handle on that. But I also wonder about the whole peer-review process—and I have brought this up for the last 20 years that I've been on this Committee—on the one hand, you want good peer reviews, because you want good, legitimate science being done. So, you want those that are knowledgeable in those areas to look at it and give their evaluation as whether or not it's legitimate, sound, and should go forward or not. It's a good system. On the other hand—on the other hand, peer reviewers tend to be those that have been in that area of scientific research for some length of time, they have all pursued certain interests. You know, maybe they're looking for the safer things, the things that they're comfortable with, that they have more understanding of. I'm often wondering, do these sort of off-the-wall kinds of things that—the new-paradigm types of research that some of you spoke about, do they—what's your comfort level

that some of these actually get through that peer-review process, these kind of really new things that maybe a peer-reviewer had never, ever been involved in before—how do they get through that?

Dr. SILICIANO. Mr. Chairman, I've had quite a bit of experience on these type of review panels, and my overall impression is that they do a really excellent job of finding the good science. There has been a mandate on these panels, for many years, to look for what's called high-risk/high-yield types of projects. My own experience is that those types of projects do get funding. The biggest—and I think the overall system works extremely well. I'd be anxious to hear what my colleagues think. But I think the problem is that the amount of funding that the system has at its disposal right now is just too low to allow the system to work effectively. When you go down from 30 percent grants being funded to——

Senator HARKIN. So, the lower the funding level, the——

Dr. SILICIANO. The whole system——

Senator HARKIN [continuing]. The increase in the safety factor tends to go up.

Dr. SILICIANO. Yes. So, I don't really think it's a problem with the mechanism, I think it's a problem with the funding.

Senator HARKIN. Yeah.

Yes, Dr. Brugge.

Dr. BRUGGE. I completely agree, but I think that, in addition, we need visionary leaders, like Dr. Zerhouni was pointing out, in terms of the nanotechnology investment. We need leaders to be aware of and make opportunities available to those individuals that are at the forefront. Because often, as you mentioned, they're—these people are—can't really be evaluated appropriately by the standing committees. So, for instance, if there's technology that is at the interface between biology and engineering, there's not really a great place—I mean, there is now, but there—initially, there wasn't a place for those grants to be reviewed. So, I think it—we do have to have extraordinary opportunity kind of funds available for the leadership at NIH and the other institutes to have RFAs in those areas so that they—we will be able to bring new ideas and new—or kind of force new—considering new options.

Senator HARKIN. Well, we had said, when we added that money, that $647 million in the continuing resolution, that some of that would be used for high-risk, high-impact research. Dr. Zerhouni has already announced those awards. New Innovators Awards. So, he's already taken that step—Dr. Zerhouni's already taken that step, and I just—but I—you know, we've often wrestled with this, over a long period of time.

Dr. BRUGGE. In our department of Cell Biology, our chairman felt very strongly that we needed better technology expertise in the Department, and so, he actually encouraged recruitment of technology experts that weren't really cell biologists. They would never have been recruited if there was a consensus vote on those individuals. But, because a slot was made for those individuals both are someone who's doing mass spectroscopy and cryoelectron microscopy, they've had more impact in our Department in our school than any other investigator. They have more collaborative papers with other individuals, and their papers are all being published in the very top journals. So, again, you need visionary leaders to be able to

highlight those types of individuals and that type of science, and bring them in, because—because of the issues that you raised, in terms of people being just comfortable where they are.

Senator HARKIN. Dr. Brugge, your statement was something I had not focused on, sort of went by me. When we're talking about the 20 percent that, for the first submission, it's about 10 percent. Is that factual now, that about——

Dr. BRUGGE. So, if you look at the chart over here—this was a chart that was just provided to me by Dr. Neiderhuber, the director of the National Cancer Institute. If you look at the yellow curve, which might be difficult to see—I asked him to specifically give me data on first submission, so all that data is on first submission—and then, to break it down into competing renewals versus new applications from either new investigators or established investigators. If you look at the yellow line, those are for competing renewals. Those are for teams that are already in place.

Senator HARKIN. Okay.

Dr. BRUGGE. Over the long haul, they've been in the range of 45 to 50 percent, but, as you can see, since 2003, there's just a precipitous drop. So, that shows that 80 percent of established investigators that are asking for renewing their team's efforts are being turned down on the first submission.

Senator HARKIN. So, that's down——

Dr. BRUGGE. And——

Senator HARKIN. But that's 20 percent.

Dr. BRUGGE. Twenty percent are being funded, 80——

Senator HARKIN. Right.

Dr. BRUGGE [continuing]. Percent are being rejected.

Senator HARKIN. Rejected. But you said for first submissions, though, it's 90/10.

Dr. BRUGGE. Okay. So, 90/10 is the overall success rate for any one cycle. So, that's a combination of the established investigators and the new investigators. So, as you can see, the new investigators are down to around 5 percent. So, the—overall 10 percent. So, for instance, NCI is funding new—or first awards from competing renewals at some—wait a minute. Okay. Maybe somebody from NCI can help with this, because it's a little complicated.

Senator HARKIN. Let me see if I can—ask it this way. Okay. So, if you take all of the first, second, third submissions and all that—so, what's the success rate? Approximately.

Dr. BRUGGE. Success rate——

Senator HARKIN. Add'em all up, and then——

Dr. BRUGGE. 20 percent.

Senator HARKIN. That's 20 percent. Take out second, third—you want first submissions. This is the first time they've submitted it.

Dr. BRUGGE. Yes. Submitted, but it could be a competitive renewal.

Senator HARKIN. Competitive renewal.

Dr. BRUGGE. It's a—you know, every 5—every 4 or 5 years, you have to——

Senator HARKIN. You have to get it renewed, right.

Dr. BRUGGE [continuing]. Get renewed. So, it could be the first submission of a competitive renewal.

Senator HARKIN. Does anyone know, or maybe Dr. Zerhouni could provide it for us—what would the success rate be just for first submissions? I don't mean renewals. I mean just for the first.

NIH SUCCESS RATE

Dr. BRUGGE. Oh. That's 5 percent.

Senator HARKIN. Oh, it's 5 percent.

Dr. ZERHOUNI. The success rate on first submissions, whether you're established or new——

Senator HARKIN. I'm going to ask Dr. Zerhouni to take a microphone.

Dr. ZERHOUNI. Dr. Brugge is right. If you come in with a new grant, the average success rate on the first submission is 10 percent. But if you are an established investigator, it's more like 17 percent.

Senator HARKIN. Yes.

Dr. ZERHOUNI. If you're a completely new investigator, it's more like 5 percent. So, on average, it's 10 percent; but it's much worse for a new investigator versus a new application from an established investigator. But, on the average, 90 percent at the first submission will have to go back and resubmit again and work on finding—on reapplying.

Senator HARKIN. I always thought that it was higher than that. I don't know why I thought——

Dr. ZERHOUNI. Right. What it is, is this, is that Dr. Brugge's talking about the first time that you submit a request——

Senator HARKIN. Right.

Dr. ZERHOUNI [continuing]. Your chances of being funded, if you're a new investigator—and this is why we really thank you for the support of new investigators—is between 5 and 7 percent.

Senator HARKIN. Now, has that been true for a long time?

Dr. ZERHOUNI. No, it has been true for the past 2–3 years.

Senator HARKIN. Okay. Good. What was it, back in the 1980s—late 1980s, early 1990s, in those areas? What happened when we doubled the funding?

Dr. ZERHOUNI. So, when you doubled the funding, the average success rate overall was about 30 percent. If you look at the statistics, you can see that the success rate for a new investigator was around 15 percent, and the success rate for an established investigator was around 40 percent. The two, together, made about 30 percent.

Senator HARKIN. So, can I—is this a correct statement I'm about to make, that—when we finished the doubling, or during that doubling, that first submissions of—first submissions—not renewals, first submissions—the approval rate would have been three times higher than it is right now—15 versus 5?

Dr. ZERHOUNI. It would have been three times higher for a new investigator.

Senator HARKIN. Yes.

Dr. ZERHOUNI. About twice as high for an established investigator.

Senator HARKIN. That's it. That—now I understand it. Hmm. Three times.

Dr. BRUGGE. That's why there's——

Senator HARKIN. Now, see——

Dr. BRUGGE [continuing]. A lot of distress.

Senator HARKIN. Now, here's another problem we get into. See, that—so, we double the funding, we get more grants out there, but obviously these grants are longer than just 3 or 4 or 5 years. They come in to get renewed. So, all the new ones that we got during the bump-up are now in the system, and they get renewed, and the new ones can't get in.

Dr. ZERHOUNI. Yes, sir, that's why we——

Senator HARKIN. I'll have to think about this one. I mean—and how we crack that. I mean, that doesn't seem to me to be the right course that we ought to be on. Obviously, the correct answer that—we talked about this doubling for a long time before we started. One of the reasons was, we had seen, over the years, how the number of peer-reviewed applications, the approval rate had gone down and down and down. We looked at each institute. Some were better than others. Some really got bad, way down, 1 in 7, 1 in 8, that kind of thing—1 in 10. The idea was to get it back up to the level so that the peer-reviewed grants would be about where we were, I don't know, 25–30 years ago. That happened. But we also wanted to make room and to encourage this new—what was that word I used? High-risk/high-impact kind of research to be done. Are we now at the point where we did the high-risk/high-impact research maybe on a one-shot basis or for a couple of years, but now we're not doing it? I mean——

Dr. STRITTMATTER. I think that's the point that I was trying to make. I think there is that influence, that, during the doubling, there was an atmosphere created where people took high risks, where things advanced rapidly. We made great strides. But the retrenchment, a backward progress in the rate of grant funding——

Senator HARKIN. Yeah.

Dr. STRITTMATTER [continuing]. Has an enormous—the biggest influence is on high-risk research and creativity in science, more——

Senator HARKIN. Sure.

Dr. STRITTMATTER [continuing]. Than steady advance.

Senator HARKIN. Sure.

Dr. STRITTMATTER. Even though—whether it's a 9-percent or 13-percent net decline in total dollars, the effect on high-risk research might be much, much greater—5, 10 times decline in these kind of crucial experiments.

Senator HARKIN. Yeah, I can understand that.

Well, I just think, Dr. Zerhouni, we're going to have to continue to work on that. On the one hand—I mean, it's both valuable. I mean, you don't want to cut off people that are in the midst of their research project. I mean, you want to continue it on, and you want to let new researchers know that, if they do get it, they're not going to be cut off at the knees once they just get established. On the other hand, you do want to encourage new people coming into the system.

Well, I think the obvious thing that strikes me is that we're simply not on a growth pattern like we ought to be on. We have to be on a growth pattern on this, and we're just not. I get the sense that a lot of people thought, "Well, we doubled it. Now we don't have

to do anything for a long time. We can just sort of sit there." I have to tell you, I hear that around here, you know, "Well, we gave you all that money once. You got all that you've got up there, so quit squawking all the time." But I don't think they realize that we were just making up for lost time, that we needed to keep that line going up.

Well, I've got a lot of questions I could ask. I don't know if Senator Specter is coming back or not right now.

One other question. You're the correct panel to ask this question to. One other thing that I want to get a better handle on is undergraduate researchers and training scientists. Now, we heard a lot during the doubling that this was going to have a ripple effect downward, even—maybe down even into high schools, getting more high school students taking science if they knew they could really become a scientist and have a career as a scientist. So, since I think most of you are all—you're all college-based, one way or the other—tell me about undergraduate researchers and scientists, and how does it look to you for the future in actually appealing to these young people to take up research and be a research scientist as a career? Because these are long-term things. That's another thing that people ask me about, "Well, you know, you don't need to do all that. I mean, if you"—it's like you can just get a researcher—just get someone to take a little time off of their practice, and they can be a researcher for a few months, and then they can go back to practice again. So, what's happening with undergraduate researchers and budding young scientists out there? You're in contact with them all the time. On the one hand, is there a desire? Do you find young people interested in the life sciences that Dr. Zerhouni talked about, this new century of life sciences? Is that interest there? Are we responding to that? Just an open—just how you feel about it.

Dr. IVERSON. Well, thank you. I'm going to take this one.

It turns out that there's nothing more transformative in science education than undergraduate research. The reason is that, in an NIH-funded laboratory doing current state-of-the-art research, an undergraduate is immersed in an environment where they finally understand what's really happening. There's no way to convey that in the lecture hall. I try my best. You can't.

Senator HARKIN. Interesting.

Dr. IVERSON. I'm here today—as I said, I'm here today because of a transformative experience. I was on my way to business school, and that event changed my thinking—not immediately, but it was because I was doing state-of-the-art research, or, you know, I was being exposed to it.

The way it generally operates is that you have laboratories that are set up, you have postdocs and graduate students, and undergraduates will come in, and they'll be working along with a graduate student or a postdoctoral fellow, be brought along slowly. What we hope is that, by the end of their second or third year, if they're excited about it, they're going to be really doing, with their own hands, research that may have an impact.

Senator HARKIN. Yeah.

Dr. IVERSON. There is nothing more transformative than this. If we don't take graduate students, we don't have those opportunities

for undergraduates. I wasn't kidding, we put 1,000 undergraduates in research opportunities at our university. We don't attempt to make 1,000 new scientists out of them. Whatever they end up doing, if they go to medical school, if they go to law school, if they do anything, they will finally understand what we have difficulty conveying in the classroom or in the media, and that is: what research is all about—the excitement, the difficulties, the real ramifications of cutting-edge research. I think that when you discuss what happens with grant funding pay lines, you have to realize that there's a very simple equation that says: fewer research opportunities for investigators translates directly into fewer research opportunities for undergraduates, as well as graduate students.

Dr. SILICIANO. I think there's another dimension to that, and that is that the undergraduates are very perceptive, and they see the environment, and they see that no matter how exciting the science is and how much fun the research is, if the principal investigator spends all of their time applying for grants and worrying about funding, that it's not an appealing sort of career choice. That's my major worry.

Senator HARKIN. Didn't you have something in your statement about how much time it took—or may time—how long it takes to—for these application processes?

Dr. SILICIANO. Yeah, I mean, traditionally it took me 30 percent, and now it's 60 percent.

Senator HARKIN. Yeah. That's a lot of time to take out just for filling out paperwork and stuff.

Dr. SILICIANO. Yeah, that's right. There's a lot less time to interact with undergraduate students, too——

Senator HARKIN. That's right.

Dr. SILICIANO [continuing]. Which is true—it is very true in my case.

Senator HARKIN. Any last things before I call a halt to this panel? Anything else that you want to bring up? Senator Specter just got the floor, I'm told, so he won't be coming back.

Dr. IVERSON. Very briefly. I would like to make one comment, and that is——

Senator HARKIN. Yes, sir.

Dr. IVERSON [continuing]. We talk about the increased grant pressure almost as a burden, and, in fact, I see it as the opposite, it's the success of the doubling that allowed us to create so many good ideas, collectively, as a scientific community that they just demand to be funded. That's what's pushing out the new ideas.

Senator HARKIN. That's good.

Dr. IVERSON. This is not a negative thing, it's a very positive thing for American science, and we just need to keep up the momentum that we've established now, as well as look toward the future with new ideas that are, right now, being pushed out.

Senator HARKIN. That was good. I like that a lot.

Well, listen, we'll close this panel down.

But now we're going to be having a press conference, with some of you, to release this study that was done, "In Our Grasp—Or Slipping Away?" So, we're going to have a press conference here. We'll close this down, and we're going to move to a press conference within just a couple of minutes.

ADDITIONAL COMMITTEE QUESTIONS

There will be some additional questions which will be submitted for your response in the record.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR TOM HARKIN

VULVODYNIA

Question. In fiscal year 2006, the Committee called upon the Office of Research on Women's Health to implement a national education program for primary care health professionals, patients and the general public on vulvodynia's symptoms, diagnosis and treatment options. I commend ORWH, under the leadership of Dr. Vivian Pinn, for its work so far to develop the campaign. Please provide an update on its current status, including a brief summary of its components, expected launch date and the resources that have been and will be allocated for this effort. Information on the resources should include the amount of funds that will be used to publicize the campaign and disseminate materials to the lay and professional communities. OD/ORWH

Answer. The Office of Research on Women's Health (ORWH), National Institutes of Health (NIH), Department of Health and Human Services (HHS), is developing a national education program for primary care health professionals, patients and the general public on vulvodynia's symptoms, diagnosis and treatment options. The first step was to initiate collaborations with relevant HHS/NIH Institutes and Centers (ICs) and key consumer and health care professional organizations through several planning meetings convened by the ORWH. Participants in on-going discussions include representatives from the National Institute of Child Health and Human Development (NICHD) and the National Institute of Neurological Disorders and Stroke (NINDS) as well as other stakeholders such as the National Vulvodynia Association (NVA), the National Women's Health Resource Center (NWHRC), the American College of Obstetricians and Gynecologists (ACOG) and interested researchers. Other Offices of Women's Health across HHS will be invited to become partners in this effort as plans for distribution of materials and additional educational efforts are developed.

A tentative launch date of this educational campaign is planned for October 2007. An initial list of documents under development includes a new ORWH Vulvodynia Fact Sheet with Questions and Answers (Q&As); a vulvodynia resource guide with relevant web site information, such as the ORWH web site for vulvodynia at http://orwh.od.nih.gov/health/vulvodynia.html; reprints of current scientific journal articles on vulvodynia, such as Vulvodynia—A State-of-the-Art Consensus on Definitions, Diagnosis and Management; and the ACOG Vulvodynia Guidelines—A Literature Review. Plans are underway to develop additional public outreach materials.

Parallel with the print material campaign will be the expansion and enhancement of the current ORWH vulvodynia web page. NICHD, the Institute that provides the majority of NIH funding for vulvodynia research, will contribute to the development and implementation of this educational effort especially through contributions of the NICHD Information Resource Center (IRC), where the materials developed will be stored and distributed for target audiences. Additionally, NICHD has offered the services of the IRC Information Specialists to answer questions in English and Spanish related to vulvodynia both online and through a 1–800 telephone line. NICHD also plans to track the labor, material, and postage for NIH vulvodynia material so that these costs can be documented.

Focus group testing will occur prior to the launch of the education campaign, including creating questions related to the materials for focus group testing, locating participants, preparing the group logistics, conducting small focus groups, and reviewing and sharing the results with the group collaborating in this effort.

Concurrent with the launch of this educational campaign, ORWH will dedicate its monthly podcast, Pinn Point on Women's Health Research, to vulvodynia, including an announcement of available materials. The podcast will also include interviews and Q&As with vulvodynia research experts and appropriate web site references for further information. The podcast will be the first step in disseminating the educational campaign. Additional plans and activities are under development. ORWH and its partners will also send html e-mail announcements to targeted organizations announcing the start of the campaign to various listserves and other internet out-

lets, as well as to women's magazine editors and other similar consumer oriented media outlets. Radio spots, produced by the NIH and widely distributed across the nation's airwaves, will also be used to focus on vulvodynia.

ORWH is developing these materials, resources, and educational plans utilizing both budgetary expenditures and in-kind contributions. For example, the contributions of the NICHD IRC will be in-kind but would ordinarily represent a significant budgetary expenditure for this project. In addition, ORWH staff time spent in development of the plan, materials and implementation of the project are not included in cost estimates.

Note: This estimate does not include dedicated ORWH staff time, NICHD staff time, or other in-kind contributions.

	Amount
ORWH Preliminary cost estimate:	
Vulvodynia Information Packet and Materials Development	$6,000
Reproduction of the vulvodynia information packet and materials (5000 copies)	115,000
Development of additional consumer information materials	30,000
Medical journal reprints	25,000
Logistical support for focus groups and direct distribution of materials	10,000
Total Estimated Cost	186,000

BEHAVIORAL RESEARCH

Question. Behavior and the environment cause more than 70 percent of avoidable deaths, suggesting that many instances of disease can be prevented. Furthermore, a recent IOM report called for the conduct of transdisciplinary research on the interactions across the genetic, behavioral, and social environments. While NIH has made great advances in understanding the genomic side of health, are there plans now to enhance research on the impact of the behavioral, social, and physical environment on health?

Answer. Building on over 50 years of behavioral and social science findings, together with recent advances in understanding genetics, NIH is poised to more fully examine the complex interactions between genetic mechanisms and environmental factors that lead to disease and disability. As noted, the recent Institute of Medicine Report, Genes, Behavior, and the Social Environment: Moving Beyond the Nature/Nurture Debate, recommends a number of ways to foster the necessary transdisciplinary research teams to accomplish this. The NIH's Office of Behavioral and Social Sciences Research (OBSSR), located in the Office of the Director, is leading the implementation of the recommendations produced by this report. Working with several NIH Institutes and Centers (ICs), OBSSR is currently developing an initiative to supplement ongoing research to allow for the addition of social environmental information to genetic studies and/or the addition of genomic information to behavioral and social science research projects. OBSSR has set aside $3 million in fiscal year 2008 for the funding of this initiative and is requesting funding contributions from the participating ICs.

OBSSR also is planning an annual genomics training institute for behavioral and social scientists. This course will cover basic concepts and methods of genomics research to better enable these investigators to integrate behavioral, social, and physical environmental factors into genomics research and thereby work more effectively with their genomics and biomedical colleagues.

In February 2006, Secretary Mike Leavitt announced the trans-NIH Genes, Environment and Health Initiative (GEI), designed to combine genetic analysis and environmental technology development to better understand the causes of common diseases. As a first step toward implementing large scale gene and environment interaction studies, a need was identified to invest in the development and improvement of tools to assess individual exposures to environmental factors and to identify biomarkers which characterize the response of these exposures on key biological pathways. OBSSR and other IC staff have been leading the effort to include social and behavioral research in this effort, resulting in research funding announcements calling for the development of measures of diet and physical activity (RFA–CA–07–032) and psychosocial stress and addictive substances (RFA–DA–07–005).

These activities are examples of recent efforts to stimulate research at the interface of genetics and the behavioral/social sciences that will ultimately allow us to examine how interactions between our genes and our environments, broadly defined to include the physical, chemical, behavioral and social environments, influence health. Nearly all ICs support investigator-initiated behavioral and social science re-

search; they also issue funding opportunity announcements to solicit research applications on particular topics, often in partnership with each other and with OBSSR. Total NIH funding for behavioral and social science research is estimated at approximately $3 billion annually since fiscal year 2004, roughly 10 percent of the entire NIH budget.

TRANSLATIONAL RESEARCH

Question. It takes years for research discoveries to reach the population at large, suggesting a significant gap in translational research. Translation of research takes place across two phases: from bench to bedside and from bedside to the population at large. What percentage of the NIH budget supports translational research overall, and how much is spent on each of the two phases?

Answer. Presently, NIH does not collect funding levels for translational research. However, we do report funding levels for clinical research, and for the current year (fiscal year 2007) and the budget year (fiscal year 2008), we estimate $8.8 billion will be spent on this research category.

QUESTIONS SUBMITTED BY SENATOR ARLEN SPECTER

REVISED MECHANISM TABLE

Question. The fiscal year 2007 enacted level provided NIH with increased funding that was not envisioned in the fiscal year 2008 Budget submission. It also requires NIH to submit a revised fiscal year 2007 operating plan. We realize increase funding in one year can impact the following year's distribution of competing grants and mechanisms. Therefore, please submit for the record a revised mechanism table that shows the impact of the fiscal year 2007 enacted level on the fiscal year 2008 President's Budget request. Also, please revise and submit any of the data in the "Tabular Data" section of NIH's Volume I Overview section of the CJ that changes to reflect the adjustments to fiscal year 2007 enacted level and its impact on the fiscal year 2008 Budget Request.

Answer. The requested revised "Tabular Data" section follows, which includes the NIH total mechanism display.

FISCAL YEAR 2006 APPROPRIATION ADJUSTMENTS

[In thousands of dollars]

IC	Cong. action		Subtotal cong. action	Real transfers					Subtotal, Pres. budget appendix
	Fiscal year			Global AIDS transfer	HHS transfer	Adv. dev. transfer	NIH RM transfer	Director's 1 percent transfer	
	2006 conference	2006 1 percent rescission							
NCI	4,841,774	−48,418	4,793,356	.....	−3,293	.....	−42,834	.....	4,747,229
NHLBI	2,951,270	−29,513	2,921,757	.....	−2,007	.....	−26,109	.....	2,893,641
NIDCR	393,269	−3,933	389,336	.....	−267	.....	−3,479	.....	385,590
NIDDK	1,722,146	−17,221	1,704,925	.....	−1,172	.....	−15,236	.....	1,688,517
NINDS	1,550,260	−15,503	1,534,757	.....	−1,054	.....	−13,715	.....	1,519,988
NIAID	4,459,395	−44,594	4,414,801	−99,000	−3,033	−49,500	−38,567	.....	4,224,701
NIGMS	1,955,170	−19,552	1,935,618	.....	−1,330	.....	−17,297	.....	1,916,991
NICHD	1,277,544	−12,775	1,264,769	.....	−869	.....	−11,302	.....	1,252,598
NEI	673,491	−6,735	666,756	.....	−458	.....	−5,958	.....	660,340
NIEHS	647,608	−6,476	641,132	.....	−440	.....	−5,729	−4,480	630,483
NIA	1,057,203	−10,572	1,046,631	.....	−719	.....	−9,353	.....	1,036,559
NIAMS	513,063	−5,131	507,932	.....	−349	.....	−4,539	.....	503,044
NIDCD	397,432	−3,974	393,458	.....	−270	.....	−3,516	.....	389,672
NIMH	1,417,692	−14,177	1,403,515	.....	−964	.....	−12,542	.....	1,390,009
NIDA	1,010,130	−10,101	1,000,029	.....	−687	.....	−8,937	.....	990,405
NIAAA	440,333	−4,403	435,930	.....	−300	.....	−3,896	.....	431,734
NINR	138,729	−1,387	137,342	.....	−94	.....	−1,227	.....	136,021
NHGRI	490,959	−4,910	486,049	.....	−334	.....	−4,343	.....	481,372
NIBIB	299,808	−2,998	296,810	.....	−204	.....	−2,652	.....	293,954
NCRR	1,110,203	−11,102	1,099,101	.....	−755	.....	−9,822	.....	1,088,524
NCCAM	122,692	−1,227	121,465	.....	−83	.....	−1,086	.....	120,296
NCMHD	197,379	−1,974	195,405	.....	−134	.....	−1,746	.....	193,525
FIC	67,048	−670	66,378	.....	−46	.....	−593	.....	65,739
NLM	318,091	−3,181	314,910	.....	−216	.....	−2,814	.....	311,880
OD	482,895	−4,829	478,066	.....	−328	.....	247,292	.....	725,030
B&F	81,900	−819	81,081	.....	−56	.....	.....	4,480	85,505
Total NIH	28,617,484	−286,175	28,331,309	−99,000	−19,462	−49,500	.....	.....	28,163,347
Superfund	80,289	−1,181	79,108	.....	.....	.....	.....	.....	79,108

FISCAL YEAR 2006 APPROPRIATION ADJUSTMENTS—Continued

[In thousands of dollars]

IC	Cong. action		Subtotal cong. action	Real transfers					Subtotal, Pres. budget appendix
	Fiscal year			Global AIDS transfer	HHS transfer	Adv. dev. transfer	NIH RM transfer	Director's 1 percent transfer	
	2006 conference	2006 1 percent rescission							
Ttl,w/Supfnd	28,697,773	−287,356	28,410,417	−99,000	−19,462	−49,500			28,242,455

IC	HHS comp. transfers		NIH comp. transfers		Other global AIDS	Subtotal HHS budg. auth.	Prog. level		Subtotal HHS table prog. level	Other NIH oblig. adjust.	Subtotal NIH CJ table
	PHSSEF pan. flu	Other HHS transfers	Roadmap comparable	Other NIH transfers			Type 1 diabetes	NLM PHS eval.			
NCI		−14	42,834	−1,872		4,788,177			4,788,177	6,896	4,795,073
NHLBI		−3	26,109	−3,824		2,915,923			2,915,923		2,915,923
NIDCR		−1	3,479	−404		388,664			388,664		388,664
NIDDK		−3	15,236	−601		1,703,149	150,000		1,853,149		1,853,149
NINDS		−3	13,715	−655		1,533,045			1,533,045		1,533,045
NIAID	18,000	−9	38,567	−1,060	99,000	4,379,199			4,379,199		4,379,199
NIGMS		−1	17,297	−244		1,934,043			1,934,043		1,934,043
NICHD		−4	11,302	−375		1,263,521			1,263,521		1,263,521
NEI		−1	5,958	−529		665,768			665,768		665,768
NIEHS		−4	5,729	−213		635,995			635,995		635,995
NIA		−3	9,353	−708		1,045,201			1,045,201		1,045,201
NIAMS		−1	4,539	−166		507,416			507,416		507,416
NIDCD		−1	3,516	−76		393,111			393,111		393,111
NIMH		−3	12,542	−735		1,401,813			1,401,813		1,401,813
NIDA		−2	8,937	−482		998,858			998,858		998,858
NIAAA		−1	3,896	−150		435,479			435,479		435,479
NINR			1,227	−98		137,150			137,150		137,150
NHGRI		−2	4,343	−58		485,655			485,655		485,655
NIBIB			2,652	1,482		298,088			298,088		298,088
NCRR			9,822	10,601		1,108,947			1,108,947		1,108,947
NCCAM			1,086	−248		121,134			121,134		121,134
NCMHD			1,746	−8		195,263			195,263		195,263
FIC			593	−15		66,317			66,317		66,317
NLM		−484	2,814	−133		314,077		8,200	322,277	1	322,278

OD	.....	−2	−247,292	571	.....	478,307	.....	.....	478,307	.....	478,307
B&F	.....	.....	.....	.....	.....	85,505	.....	.....	85,505	.....	85,505
Total NIH	18,000	−542	.....	.....	99,000	28,279,805	150,000	8,200	28,438,005	6,897	28,444,902
Superfund	.....	.....	.....	.....	.....	79,108	.....	.....	79,108	.....	79,108
Ttl,w/Supfnd	18,000	−542	.....	.....	99,000	28,358,913	150,000	8,200	28,517,113	6,897	28,524,010

FISCAL YEAR 2007 ADJUSTMENTS—JOINT RESOLUTION LEVEL

[In thousands of dollars]

IC	Joint resolution	Comp. trnsf. advanced dev.	Subtotal, Pres. budget appendix	Other HHS transfers	NIH comp. transfers	Subtotal, HHS budg. auth.	Prog. level		Subtotal, HHS prog. level
							Type I diabetes	NLM PHS Eval.	
NCI	$4,797,639	.....	$4,797,639	−$14	−$2,134	$4,795,491	.....	.....	$4,795,491
NHLBI	2,922,929	.....	2,922,929	−3	−2,946	2,919,980	.....	.....	2,919,980
NIDCR	389,703	.....	389,703	−1	−332	389,370	.....	.....	389,370
NIDDK	1,705,868	.....	1,705,868	−3	−639	1,705,226	$150,000	.....	1,855,226
NINDS	1,535,545	.....	1,535,545	−3	−638	1,534,904	.....	.....	1,534,904
NIAID	4,417,208	−$49,500	4,367,708	−9	−1,254	4,366,445	.....	.....	4,366,445
NIGMS	1,935,808	.....	1,935,808	−1	−182	1,935,625	.....	.....	1,935,625
NICHD	1,254,707	.....	1,254,707	−4	−559	1,254,144	.....	.....	1,254,144
NEI	667,116	.....	667,116	−1	−440	666,675	.....	.....	666,675
NIEHS	642,002	.....	642,002	−4	−225	641,773	.....	.....	641,773
NIA	1,047,260	.....	1,047,260	−3	−757	1,046,500	.....	.....	1,046,500
NIAMS	508,240	.....	508,240	−1	−179	508,060	.....	.....	508,060
NIDCD	393,668	.....	393,668	−1	−127	393,540	.....	.....	393,540
NIMH	1,404,494	.....	1,404,494	−3	−921	1,403,570	.....	.....	1,403,570
NIDA	1,000,621	.....	1,000,621	−2	−605	1,000,014	.....	.....	1,000,014
NIAAA	436,259	.....	436,259	−1	−201	436,057	.....	.....	436,057
NINR	137,404	.....	137,404	.....	−117	137,287	.....	.....	137,287
NHGRI	486,491	.....	486,491	−2	−62	486,427	.....	.....	486,427
NIBIB	296,887	.....	296,887	.....	1,504	298,391	.....	.....	298,391
NCRR	1,133,240	.....	1,133,240	.....	10,601	1,143,841	.....	.....	1,143,841
NCCAM	121,576	.....	121,576	.....	−197	121,379	.....	.....	121,379
NCMHD	199,444	.....	199,444	.....	−15	199,429	.....	.....	199,429
FIC	66,446	.....	66,446	.....	−24	66,422	.....	.....	66,422
NLM	320,850	.....	320,850	−484	−137	320,229	.....	$8,200	328,429

FISCAL YEAR 2007 ADJUSTMENTS—JOINT RESOLUTION LEVEL—Continued

[In thousands of dollars]

IC	Joint resolution	Comp. trnsf. advanced dev.	Subtotal, Pres. budget appendix	Other HHS transfers	NIH comp. transfers	Subtotal, HHS budg. auth.	Prog. level		Subtotal, HHS prog. level
							Type I diabetes	NLM PHS Eval.	
OD	1,096,401	.....	1,096,401	−2	586	1,096,985	.....	.....	1,096,985
B&F	81,081	.....	81,081	.....	.....	81,081	.....	.....	81,081
Total NIH	28,998,887	−49,500	28,949,387	−542	.....	28,948,845	150,000	8,200	29,107,045
Superfund	79,117	.....	79,117	.....	.....	79,117	.....	.....	79,117
Total, w/Supfnd	29,078,004	−49,500	29,028,504	−542	.....	29,027,962	150,000	8,200	29,186,162

FISCAL YEAR 2008 PRESIDET'S BUDGET REQUEST

Appropriation	Fiscal year				
	2006 actual [1 2 3 4 5 6]	2007 Presidet's budget [1 3 4 5 6]	2007 joint resolution [1 3 4 5 6]	2008 Presidet's budget [1]	2008 Est. +/− 2007 joint resolution
NCI	$4,795,073,000	$4,751,461,000	$4,795,491,000	$4,782,114,000	−$13,377,000
NHLBI	2,915,923,000	2,898,063,000	2,919,980,000	2,925,413,000	+5,433,000
NIDCR	388,664,000	385,762,000	389,370,000	389,722,000	+352,000
NIDDK [7]	1,853,149,000	1,843,656,000	1,855,226,000	1,858,045,000	+2,819,000
NINDS	1,533,045,000	1,524,109,000	1,534,904,000	1,537,019,000	+2,115,000
NIAID	[8 9] 4,379,199,000	4,394,233,000	[9] 4,366,445,000	4,592,482,000	+226,037,000
NIGMS	1,934,043,000	1,923,298,000	1,935,625,000	1,941,462,000	+5,837,000
NICHD	1,263,521,000	1,256,855,000	1,254,144,000	1,264,946,000	+10,802,000
NEI	665,768,000	660,917,000	666,675,000	667,820,000	+1,145,000
NIEHS	[10] 635,995,000	637,094,000	641,773,000	637,406,000	−4,367,000
NIA	1,045,201,000	1,039,068,000	1,046,500,000	1,047,148,000	+648,000
NIAMS	507,416,000	504,353,000	508,060,000	508,082,000	+22,000
NIDCD	393,111,000	391,428,000	393,540,000	393,682,000	+142,000
NIMH	1,401,813,000	1,393,882,000	1,403,570,000	1,405,421,000	+1,851,000
NIDA	998,858,000	994,222,000	1,000,014,000	1,000,365,000	+351,000
NIAAA	435,479,000	433,116,000	436,057,000	436,505,000	+448,000
NINR	137,150,000	136,433,000	137,287,000	137,800,000	+513,000
NHGRI	485,655,000	482,878,000	486,427,000	484,436,000	−1,991,000

NIBIB	298,088,000	296,354,000	298,391,000	300,463,000	+2,072,000
NCRR	1,108,947,000	1,108,843,000	1,143,841,000	1,112,498,000	−31,343,000
NCCAM	121,134,000	120,357,000	121,379,000	121,699,000	+320,000
NCMHD	195,263,000	194,284,000	199,429,000	194,495,000	−4,934,000
FIC	66,317,000	66,657,000	66,422,000	66,594,000	+172,000
NLM [12]	314,078,000	312,648,000	320,229,000	312,562,000	−7,667,000
OD [13]	478,307,000	[11] 508,909,000	1,096,985,000	517,062,000	−579,923,000
B&F	[10] 85,505,000	81,081,000	81,081,000	136,000,000	+54,919,000
Type 1 Diabetes	−150,000,000	−150,000,000	−150,000,000	−150,000,000	
Subtotal, Labor/HHS	28,286,702,000	28,189,961,000	28,948,845,000	28,621,241,000	−327,604,000
Interior/Superfund Research Program	79,108,000	78,414,000	79,117,000	78,434,000	−683,000
Total, NIH Discretioary B.A	28,365,810,000	28,268,375,000	29,027,962,000	28,699,675,000	−328,287,000
Type 1 Diabetes [7]	150,000,000	150,000,000	150,000,000	150,000,000	
Total, NIH Budget Authority	28,515,810,000	28,418,375,000	29,177,962,000	28,849,675,000	−328,287,000
NLM Program Evaluation	8,200,000	8,200,000	8,200,000	8,200,000	
Total, Prog. Level	28,524,010,000	28,426,575,000	29,186,162,000	28,857,875,000	−328,287,000

[1] Includes funds to be transferred to the Global Fund for HIV/AIDS, Malaria, and Tuberculosis (fiscal year 2006—$99,000,000; fiscal year 2007 PB—$100,000,000; fiscal year 2007 Annualized—$99,000,000; fiscal year 2008—$300,000,000).
[2] Includes Government-wide 1 percent rescission and HHS 1 percent transfer.
[3] Comparable for ASAM and ASPA transfer—$62,000.
[4] Comparable for DBEPS program transfer to NIBIB (fiscal year 2006—$1,496,000; fiscal year 2007—$1,528,000).
[5] Comparable for CIO transfer to OD (fiscal year 2006—$641,000; fiscal year 2007—$669,000).
[6] Comparable for K–30 transfer to NCRR ($10,613,000).
[7] Includes funds for the Type 1 Diabetes Initiative.
[8] NIAID includes $18,000,000 for Pandemic Influenza from PHSSEF.
[9] Comparable for transfer of Advance Development Fund to ASPR (−$49,500,000).
[10] Directors 1 percent transfer NIEHS to B&F ($4,480,000).
[11] OD comparable (−$159,500,000) to ASPR for Advance Development Fund.
[12] Comparable for transfer to DHHS for PHS Historian ($480,000).
[13] Total OD includes Roadmap funds for fiscal year 2006 of $82,170,000; fiscal year 2007 PB of $110,700,000; fiscal year 2007 Annualized Current Rate of $82,170; fiscal year 2008 of $121,540,000.

BUDGET MECHANISM—TOTAL

[Dollars in thousands]

MECHANISM	Fiscal year								Change		Percent change amount
	2006 actual [1]		2007 revised Pres. budget		2007 joint resolution		2008 estimate		No	Amount	
	No	Amount	No	Amount	No	Amount	No	Amount			
Research Grants											
Research Projects:											
Noncompeting	27,366	$11,070,308	26,669	$11,063,137	26,668	$10,896,993	26,573	$10,975,609	−95	$78,616	0.7
Administrative supplements	(1,678)	284,083	(1,254)	145,687	(1,463)	177,707	(1,543)	204,463	(80)	26,756	15.1
Competing	9,129	3,361,827	9,290	3,384,714	10,154	3,731,558	9,404	3,293,817	(750)	−437,741	−11.7
Subtotal, RPGs	36,495	14,716,218	35,959	14,593,538	36,822	14,806,258	35,977	14,473,889	−845	−332,369	2.2
SBIR/STTR	1,822	616,779	1,829	605,284	1,807	610,998	1,793	606,930	−14	−4,068	−0.7
Subtotal, RPGs	38,317	15,332,997	37,788	15,198,822	38,629	15,417,256	37,770	15,080,819	−859	−336,437	2.2
Research Centers:											
Specialized/comprehensive	1,190	2,144,310	1,104	2,147,862	1,114	2,196,970	1,108	2,198,277	−6	1,307	0.1
Clinical research	93	348,476	295	375,986	95	386,898	89	419,123	−6	32,225	8.3
Biotechnology	103	134,862	113	133,797	113	134,345	111	130,550	−2	−3,795	−2.8
Comparative medicine	51	123,032	49	122,294	49	123,019	47	117,735	−2	−5,284	−4.3
Research Centers in Minority Institutions	28	54,213	28	53,289	28	53,819	27	51,727	−1	−2,092	−3.9
Subtotal, Centers	1,465	2,804,893	1,589	2,833,228	1,399	2,895,051	1,382	2,917,412	−17	22,361	0.8
Other Research:											
Research careers	4,192	644,693	4,322	674,060	4,425	693,226	4,540	700,715	115	7,489	1.1
Cancer education	99	34,561	99	34,406	102	35,406	103	35,806	1	400	1.1
Cooperative clinical research	353	344,503	351	344,249	368	353,445	364	354,580	−4	1,135	0.3
Biomedical research support	140	65,518	139	64,312	212	98,312	139	61,745	−73	−36,567	−37.25
Minority biomedical research support	155	115,032	151	114,470	149	113,810	158	112,630	9	−1,180	−1.0
Other	1,685	465,044	1,648	469,711	1,722	473,598	1,708	481,691	−14	8,093	1.7

Subtotal, Other Research	6,624	1,669,351	6,710	1,701,208	6,978	1,767,797	7,012	1,747,167	34	−20,630	−1.2
Total Research Grants	46,406	19,807,241	46,087	19,733,258	47,006	20,080,104	46,164	19,745,398	−842	−334,706	−1.7
Ruth L. Kirschstein Training Awards:											
Individual awards	[2] 2,976	122,758	[2] 2,995	124,192	[2] 3,081	127,983	[2] 3,078	127,728	−3	−255	−0.2
Institutional awards	[2] 14,349	625,883	[2] 14,461	631,604	[2] 14,663	643,617	[2] 14,583	641,685	−80	−1,932	−0.3
Total, Training	[2] 17,325	748,641	[2] 17,456	755,796	[2] 17,744	771,600	[2] 17,661	769,413	−83	−2,187	−0.3
Research & development contracts	3,423	2,667,066	3,460	2,652,882	3,529	2,783,528	3,552	2,975,285	23	191,757	6.9
(SBIR/STTR)	(92)	(23,809)	(98)	(24,504)	(110)	(30,027)	(110)	(29,996)	.....	(−31)	−0.1
Intramural research	.....	2,772,036	.....	2,751,751	.....	2,791,706	.....	2,774,311	.....	−17,395	−0.6
Research management and support	.....	1,108,615	.....	1,122,498	.....	1,132,127	.....	1,142,492	.....	10,365	0.9
Cancer prevention & control	.....	505,705	.....	502,700	.....	516,565	.....	516,565	.....	.....	.....
Extramural Construction	.....	29,700	.....	25,000	.....	.....	.....	.....	.....	.....	.....
Library of Medicine	.....	311,264	.....	308,866	.....	320,229	.....	308,415	.....	−11,814	−3.7
(Appropriation)	.....	(314,078)	.....	(312,648)	.....	(320,229)	.....	(312,562)	.....	(−7,667)	−2.4
Office of the Director	.....	393,009	.....	398,209	.....	613,985	.....	395,522	.....	−218,463	−35.6
(Appropriation)	.....	(478,307)	.....	(508,909)	.....	(1,096,985)	.....	(517,062)	.....	(−579,923)	−52.9
Buildings and Facilities [3]	.....	93,425	.....	89,001	.....	89,001	.....	143,840	.....	54,839	61.6
(Appropriation)	.....	(85,505)	.....	(81,081)	.....	(81,081)	.....	(136,000)	.....	(54,919)	67.7
NIH Roadmap for Medical Research [4]	.....	(332,590)	.....	(442,673)	.....	(483,000)	.....	(486,153)	.....	(3,153)	0.7
Type 1 Diabetes [5]	.....	−150,000	.....	−150,000	.....	−150,000	.....	−150,000	.....	.....	.....
Subtotal, Labor/HHS Budget Authority	.....	28,286,702	.....	28,189,961	.....	28,948,845	.....	28,621,241	.....	−327,604	−1.1
Interior Appropriation for Superfund Res	.....	79,108	.....	78,414	.....	79,117	.....	78,434	.....	−683	−0.9
Total, NIH Discretionary B.A	.....	28,365,810	.....	28,268,375	.....	29,027,962	.....	28,699,675	.....	−328,287	−1.1
Type 1 Diabetes [5]	.....	150,000	.....	150,000	.....	150,000	.....	150,000	.....	.....	.....
Total, NIH Budget Authority	.....	28,515,810	.....	28,418,375	.....	29,177,962	.....	28,849,675	.....	−328,287	−1.1

BUDGET MECHANISM—TOTAL—Continued

[Dollars in thousands]

MECHANISM	Fiscal year								Change		Percent change amount
	2006 actual [1]		2007 revised Pres. budget		2007 joint resolution		2008 estimate		No	Amount	
	No	Amount	No	Amount	No	Amount	No	Amount			
NLM Program Evaluation	.....	8,200	.....	8,200	.....	8,200	.....	8,200	.....	.....	.....
Total, Program Level	.....	28,524,010	.....	28,426,575	.....	29,186,162	.....	28,857,875	.....	−328,287	−1.1

[1] Budget Authority 2006 total includes mechanism distribution of NCI breast cancer stamp funds of $6,896.

[2] FTTPs.

[3] Includes the B&F appropriation plus the following included in NCI—fiscal year 2006: $7,920; fiscal year 2007: $7,920; fiscal year 2008: $7,840.

[4] Included in above mechanisms. Roadmap contributions from the NLM and OD are reflected in the mechanisms of award.

[5] Included in NIDDK—fiscal year 2006: $150,000; fiscal year 2007: $150,000; fiscal year 2008: $150,000.

Numbers of grants identified in fiscal year 2007 and fiscal year 2008 are estimates, and WILL change as applications are received and selected for funding.

Fiscal year 2006 and fiscal year 2007 have been adjusted to display comparably proposed program changes in fiscal year 2008. The fiscal year 2008 President's Budget Appendix reflects an actual fiscal year 2006 budget authority total of $28,242 million, a difference of $282 million from the fiscal year 2006 program level reported above. fiscal year 2006 adjustments to the Budget Appendix include the addition of Special Statutory Type I Diabetes Funds +$150M); a transfer from the PHSSEF for Pandemic Influenza activities (+$18M); a comparable adjustment for the Global Fund for HIV/AIDS actual transfer (+$99M); revenue from the Breast Cancer Stamp (+$7M);and use of the Secretary's evaluation funds transfer authority for NLM (+$8M). The fiscal year 2007 budget authority in the fiscal year 2008 Budget Appendix is $28,450 million, a difference of $736 million from the fiscal year 2007 Joint Resolution program level reported above. In addition to increases provided by the fiscal year 2007 Joint Resolution, fiscal year 2007 program level adjustments include the addition of Special Statutory Type I Diabetes Funds (+$150M); and use of the Secretary's evaluation funds transfer authority for NLM (+$8M).

FISCAL YEAR 2008 SPECIAL INITIATIVES

[In thousands of dollars]

	Pathway to independence	CTSA
NCI	1,800	.....
NHLBI	1,980	.....
NIDCR	540	.....
NIDDK	1,080	.....
NINDS	1,170	.....
NIAID	540	.....
NIGMS	1,350	.....
NICHD	900	.....
NEI	360	.....
NIEHS	900	.....
NIA	630	.....
NIAMS	360	.....
NIDCD	360	.....
NIMH	900	.....
NIDA	540	.....
NIAAA	270	.....
NINR	180	.....
NHGRI	270	.....
NIBIB	450	.....
NCRR	90	10,000
NCCAM	180	.....
NCMHD	270	.....
FIC	180	.....
NLM	450	.....
Total	15,750	10,000

CTSA = Clinical Translational Science Awards

APPROPRIATION HISTORY

Fiscal year	Budget request to Congress	House allowance	Senate allowance	Appropriation [1]
1999	[2] $14,763,313,000	$14,862,023,000	$15,622,386,000	[3] $15,629,156,000
2000	[4] 15,932,786,000	16,964,547,000	17,613,470,000	[5] 17,820,587,000
2001	[6] 18,812,735,000	20,512,735,000	20,512,735,000	[7] [8] 20,458,130,000
2002	23,112,130,000	22,945,199,000	23,765,488,000	[9] [10] [11] 23,296,382,000
2003	[12] 27,343,417,000	27,351,717,000	27,369,000,000	[13] 27,066,782,000
2004	27,892,765,000	28,043,991,000	28,369,548,000	[14] 27,887,512,000
2005	28,757,357,000	28,657,357,000	28,901,185,000	[15] 28,495,157,000
2006	28,740,073,000	28,737,094,000	29,644,804,000	[16] 28,461,417,000
2007	28,578,417,000	[17] 28,479,417,000	[17] 28,779,081,000	[18] 29,228,004,000
2008	28,849,675,000	.....	.....	.....

[1] Reflects enacted supplementals, rescissions and reappropriations.
[2] Reflects a decrease of $34,530,000 for the budget amendment for bioterrorism. Includes $1,728,099,000 for HIV research in the NIH Office of AIDS Research.
[3] Includes $1,800,046,000 appropriated to the ICs for HIV research. Includes $10,230,000 for rescission.
[4] Includes $1,833,826,000 for HIV research in the NIH Office of AIDS Research. Includes $40 million appropriated in fiscal year 1999 for the Clinical Research Center.
[5] Includes $2,024,956,000 appropriated to the ICs for HIV research. Includes $99,883,000 for NIH share of across-the-board reduction and reflects $20,000,000 transferred to CDC. Includes $40,000,000 in forward funding appropriated in fiscal year 1999.
[6] Includes $2,111,224,000 for HIV research in the NIH Office of AIDS Research.
[7] Includes $2,244,987,000 appropriated to the ICs for HIV research. Reflects NIH share of across-the-board reduction ($8,666,000) and $5,800,000 transferred to the DHHS.
[8] In fiscal year 2001, NIH began receiving a separate appropriation for Superfund Research activities at NIEHS.
[9] Includes $2,535,672,000 appropriated to the ICs for HIV research. Reflects NIH share of across-the-board reduction ($9,273,000), Labor/HHS ($22,946,000) and government-wide ($34,243,000) rescissions, and transfer of $100M to the Global Fund for HIV/AIDS, malaria, and tuberculosis.
[10] Includes $10.5 million appropriated from the Emergency Relief Fund.
[11] Beginning with the fiscal year 2002 Appropriation, includes amounts authorized to the NIDDK for Type 1 diabetes research.
[12] Excludes $583,000 transferred to the Department of Homeland Security.
[13] Includes $2,747,463,000 appropriated to the ICs for HIV research. Reflects NIH share of the across-the-board reduction ($177,085,000), and transfers of $99,350,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis, and $583,000 to the Department of Homeland Security.
[14] Includes $2,850,581,000 appropriated to the ICs for HIV research. Reflects NIH share of across-the-board reduction ($165,459,000), Labor/HHS rescission ($17,492,000), and transfer of $149,115,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis.
[15] Includes $2,920,551,000 appropriated to the ICs for HIV research. Reflects NIH share of across-the-board reduction ($229,390,000), Labor/HHS rescission ($6,787,000), and transfer of $99,200,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis.
[16] Includes $2,903,664,000 appropriated to the ICs for HIV research. Reflects NIH share of the Government-wide rescission ($287,356,000), and transfer of $99,000,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis.
[17] Reflects funding levels approved by the Appropriations Committees. Neither chamber had passed the Labor/HHS appropriations bill at the time this budget was prepared.
[18] Joint Resolution.

HISTORY OF CONGRESSIONAL APPROPRIATIONS, FISCAL YEARS 1998–2007

[In thousands of dollars]

Fiscal year	NCI	NHLBI	NIDCR	NIDDK	NINDS	NIAID	NIGMS	NICHD	NEI	NIEHS	NIA	NIAMS	NIDCD	NIMH
1998	2,547,314	1,531,061	209,415	900,860	780,713	1,351,655	1,065,947	674,766	355,691	330,108	519,279	274,760	200,695	750,241
1999	2,925,247	1,792,509	234,183	1,020,559	902,680	1,569,063	1,197,026	750,485	395,595	375,494	596,126	307,960	229,735	860,638

2000	3,314,554	2,029,424	268,811	1,168,476	1,029,376	1,778,038	1,354,420	858,291	450,300	442,449	686,479	349,968	263,771	973,146
2001	3,754,456	2,298,512	306,211	1,399,684	1,175,854	2,041,698	1,535,378	975,766	510,352	564,810	785,590	396,460	300,418	1,106,305
2002	4,181,233	2,572,667	342,664	1,562,144	1,326,666	2,342,313	1,724,799	1,111,674	580,713	645,422	892,267	448,248	341,675	1,246,640
2003	4,592,348	2,793,733	371,636	1,722,730	1,456,476	3,606,789	1,847,000	1,205,927	633,148	697,767	993,598	486,143	370,382	1,341,014
2004	4,739,255	2,878,691	383,282	1,821,803	1,501,207	4,155,447	1,904,838	1,242,361	653,052	710,701	1,024,754	501,066	382,053	1,381,774
2005	4,825,258	2,941,201	391,829	1,863,584	1,539,448	4,303,641	1,944,067	1,270,321	669,070	724,347	1,051,990	511,157	394,260	1,411,933
2006	4,793,356	2,921,757	389,336	1,854,925	1,534,757	4,315,801	1,935,618	1,264,769	666,756	720,240	1,046,631	507,932	393,458	1,403,515
2007	4,797,639	2,922,929	389,703	1,855,868	1,535,545	4,417,208	1,935,808	1,254,707	667,116	721,119	1,047,260	508,240	393,668	1,404,494

Fiscal year	NIDA	NIAAA	NINR	NHGRI	NIBIB	NCRR	NCCAM	NCMHD	FIC	NLM	OD	B&F	OAR	TOTAL
1998	527,175	227,175	63,597	217,704	.....	453,883	.....	.....	28,289	161,185	296,373	206,957	.....	[1] 13,674,843
1999	602,874	259,575	69,788	264,707	.....	554,446	.....	.....	35,402	181,189	306,356	197,519	.....	[2] 15,629,156
2000	685,781	292,369	89,522	335,527	.....	676,557	68,390	.....	43,494	214,068	282,000	165,376	.....	[3] 17,820,587
2001	780,833	340,453	104,328	382,112	.....	817,253	89,138	130,096	50,482	246,351	211,800	153,790	.....	[4] 20,458,130
2002	886,718	383,615	120,366	428,758	111,861	1,011,262	104,451	157,563	56,859	276,091	235,113	204,600	.....	[5] 23,296,382
2003	961,721	416,051	130,584	464,995	278,279	1,138,821	113,407	185,714	163,465	300,135	266,232	628,687	.....	[6] 27,066,782
2004	990,953	428,669	134,724	479,073	287,129	1,179,058	116,978	191,471	65,382	317,315	327,504	88,972	.....	[7] 27,887,512
2005	1,006,419	438,277	138,072	488,608	298,209	1,115,090	122,105	196,159	66,632	315,146	358,046	110,288	.....	[8] 28,495,157
2006	1,000,029	435,930	137,342	486,049	296,810	1,099,101	121,465	195,405	66,378	314,910	478,066	81,081	.....	[9] 28,461,417
2007	1,000,621	436,259	137,404	486,491	296,887	1,133,240	121,576	199,444	66,446	320,850	1,096,401	81,081	.....	[10] 29,228,004

[1] Funds for HIV research in the amount of $1,607,053,000 appropriated to the ICs. Beginning in fiscal year 1998, includes funds appropriated to NIDDK for Type 1 diabetes research.

[2] Funds for HIV research in the amount of $1,800,046,000 appropriated to the ICs. Reflects rescission of $10,230,000.

[3] Funds for HIV research in the amount of $2,024,956 appropriated to the ICs. Reflects NIH share of across-the-board reduction ($99,883,000) and transfer to CDC ($20,000,000). Includes $40,000,000 in forward funding appropriated in fiscal year 1999.

[4] Funds for HIV research in the amount of $2,244,987,000 appropriated to the ICs. Reflects NIH share of across-the-board reduction ($8,666,000) and transfer to DHHS ($5,800,000). In fiscal year 2001, NIH began receiving a separate appropriation for Superfund Research activities at NIEHS.

[5] Funds for HIV research in the amount of $2,535,672,000 appropriated to the ICs. Reflects NIH share of across-the-board reduction ($9,273,000), Labor/HHS ($22,946,000) and government-wide ($34,243,000) rescissions, and transfer of $100M to the Global Fund for HIV/AIDS, malaria, and tuberculosis.

[6] Funds for HIV research in the amount of $2,747,463,000 appropriated to the ICs. Reflects NIH share of across-the-board reduction ($177,085,000), and transfers of $99,350,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis, and $583,000 to the Department of Homeland Security.

[7] Funds for HIV research in the amount of $2,850,581,000 appropriated to the ICs. Reflects NIH share of across-the-board reduction ($165,459,000), Labor/HHS rescission ($17,492,000), and transfer of $149,115,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis.

[8] Funds for HIV research in the amount of $2,920,551,000 appropriated to the ICs. Reflects NIH share of across-the-board reduction ($229,390,000), Labor/HHS rescission ($6,787,000), and transfer of $99,200,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis.

[9] Funds for HIV research in the amount of $2,903,664,000 appropriated to the ICs. Reflects NIH share of the Government-wide rescission ($287,356,000), and transfer of $99,000,000 to the Global Fund for HIV/AIDS, malaria, and tuberculosis.

[10] Joint Resolution.

FULL-TIME EQUIVALENTS

Institutes and Centers	Fiscal year		
	2006 actual	2007 Joint resolution	2008 President's budget
NCI	2,777	2,835	2,875
NHLBI	797	806	817
NIDCR	245	252	256
NIDDK	638	646	655
NINDS	526	539	547
NIAID	1,589	1,617	1,639
NIGMS	125	126	129
NICHD	547	548	557
NEI	207	213	215
NIEHS	664	668	677
NIA	378	381	386
NIAMS	211	214	217
NIDCD	133	136	138
NIMH	616	641	651
NIDA	361	366	371
NIAAA	225	227	230
NINR	43	44	45
NHGRI	292	301	305
NIBIB	48	50	51
NCRR	99	108	109
NCCAM	74	76	77
NCMHD	25	29	31
FIC	52	54	55
Subtotals, ICs	10,672	10,877	11,033
NLM	656	662	671
OD	578	630	638
Central Services	4,966	5,037	5,107
Subtotal, NIH	16,872	17,206	17,449
Undistributed	.....	.....	.....
Ceiling exempt [1]	8	10	10
Total, NIH	16,880	17,216	17,459

[1] CRADA FTEs are supported by Cooperative Research and Development Agreements

BUDGET AUTHORITY BY OBJECT [1]

	Object Classes	Fiscal year		Increase or decrease
		2007 Joint Resolution	2008 estimate	
	Personnel Compensation:			
11.1	Full-Time Permanent	$838,033,000	$881,383,000	$43,350,000
11.3	Other than Full-Time Permanent	263,580,000	276,142,000	12,562,000
11.5	Other Personnel Compensation	29,783,000	31,112,000	1,329,000
11.7	Military Personnel	26,032,000	27,721,000	1,689,000
11.8	Special Personnel Services Payments	171,584,000	175,795,000	4,211,000
	Total, Personnel Compensation	1,329,012,000	1,392,153,000	63,141,000
12.1	Civilian Personnel Benefits	311,004,000	326,309,000	15,305,000
12.2	Military Personnel Benefits	17,255,000	18,026,000	771,000
13.0	Benefits for Former Personnel	.....	.....	.....
	Subtotal, Pay Costs	1,657,271,000	1,736,488,000	79,217,000
21.0	Travel & Transportation of Persons	55,429,000	52,639,000	(2,790,000)
22.0	Transportation of Things	5,174,000	4,938,000	(236,000)
23.1	Rental Payments to GSA	64,000	61,000	(3,000)
23.2	Rental Payments to Others	1,380,000	1,373,000	(7,000)

BUDGET AUTHORITY BY OBJECT [1]—Continued

	Object Classes	Fiscal year		Increase or decrease
		2007 Joint Resolution	2008 estimate	
23.3	Communications, Utilities & Miscellaneous Charges	29,949,000	29,770,000	(179,000)
24.0	Printing & Reproduction	14,418,000	14,093,000	(325,000)
25.1	Consulting Services	120,471,000	117,621,000	(2,850,000)
25.2	Other Services	515,643,000	485,772,000	(29,871,000)
25.3	Purchase of Goods & Services from Government Accounts	2,526,800,000	2,508,161,000	(18,639,000)
25.4	Operation & Maintenance of Facilities	297,892,000	263,545,000	(34,347,000)
25.5	Research & Development Contracts	2,140,434,000	2,315,525,000	175,091,000
25.6	Medical Care	16,482,000	16,110,000	(372,000)
25.7	Operation & Maintenance of Equipment	76,450,000	72,506,000	(3,944,000)
25.8	Subsistence & Support of Persons	.....	.....	.....
25.0	Subtotal, Other Contractual Services	5,694,172,000	5,779,240,000	85,068,000
26.0	Supplies & Materials	216,416,000	201,809,000	(14,607,000)
31.0	Equipment	126,456,000	119,236,000	(7,220,000)
32.0	Land and Structures	.....	.....	.....
33.0	Investments & Loans	.....	.....	.....
41.0	Grants, Subsidies & Contributions	21,297,989,000	20,831,478,000	(466,511,000)
42.0	Insurance Claims & Indemnities	10,000	10,000	.....
43.0	Interest & Dividends	117,000	106,000	(11,000)
44.0	Refunds	.....	.....	.....
	Subtotal, Non-Pay Costs	27,441,574,000	27,034,753,000	(406,821,000)
	Total Budget Authority by Object	29,098,845,000	28,771,241,000	(327,604,000)

[1] Reflects request to Labor/HHS/Education Subcommittee, and includes Type 1 Diabetes funds provided through Public Law 107–360.

BUDGET AUTHORITY BY OBJECT INCLUDING SERVICE AND SUPPLY FUND AND MANAGEMENT FUND [1]

	Object Classes	Fiscal year		Increase or Decrease
		2007 Joint Resolution	2008 Estimate	
	Personnel Compensation:			
11.1	Full-Time Permanent	$1,115,616,000	$1,168,343,000	$52,727,000
11.3	Other than Full-Time Permanent	339,113,000	353,676,000	14,563,000
11.5	Other Personnel Compensation	48,648,000	50,402,000	1,754,000
11.7	Military Personnel	35,988,000	37,905,000	1,917,000
11.8	Special Personnel Services Payments	175,535,000	179,832,000	4,297,000
	Total, Personnel Compensation	1,714,900,000	1,790,158,000	75,258,000
12.1	Civilian Personnel Benefits	416,629,000	434,651,000	18,022,000
12.2	Military Personnel Benefits	21,800,000	22,647,000	847,000
13.0	Benefits for Former Personnel	661,000	672,000	11,000
	Subtotal, Pay Costs	2,153,990,000	2,248,128,000	94,138,000
21.0	Travel & Transportation of Persons	58,562,000	56,236,000	(2,326,000)
22.0	Transportation of Things	6,602,000	6,369,000	(233,000)
23.1	Rental Payments to GSA	40,154,000	40,402,000	248,000
23.2	Rental Payments to Others	85,139,000	85,657,000	518,000
23.3	Communications, Utilities & Miscellaneous Charges	148,541,000	149,124,000	583,000
24.0	Printing & Reproduction	21,749,000	21,448,000	(301,000)
25.1	Consulting Services	136,456,000	133,654,000	(2,802,000)
25.2	Other Services	1,002,883,000	974,048,000	(28,835,000)
25.3	Purchase of Goods & Services from Government Accounts	858,478,000	821,161,000	(37,317,000)
25.4	Operation & Maintenance of Facilities	415,313,000	381,429,000	(33,884,000)
25.5	Research & Development Contracts	2,143,108,000	2,318,213,000	175,105,000

BUDGET AUTHORITY BY OBJECT INCLUDING SERVICE AND SUPPLY FUND AND MANAGEMENT FUND [1]—Continued

	Object Classes	Fiscal year		Increase or Decrease
		2007 Joint Resolution	2008 Estimate	
25.6	Medical Care	24,463,000	23,703,000	(760,000)
25.7	Operation & Maintenance of Equipment	173,642,000	170,147,000	(3,495,000)
25.8	Subsistence & Support of Persons	.....	.....	.....
25.0	Subtotal, Other Contractual Services	4,754,343,000	4,822,355,000	68,012,000
26.0	Supplies & Materials	336,691,000	321,810,000	(14,881,000)
31.0	Equipment	194,842,000	188,002,000	(6,840,000)
32.0	Land and Structures	77,000	77,000	.....
33.0	Investments & Loans	.....	.....	.....
41.0	Grants, Subsidies & Contributions	21,297,989,000	20,831,478,000	(466,511,000)
42.0	Insurance Claims & Indemnities	14,000	14,000	.....
43.0	Interest & Dividends	152,000	141,000	(11,000)
44.0	Refunds	.....	.....	.....
	Subtotal, Non-Pay Costs	26,944,855,000	26,523,113,000	(421,742,000)
	Total Budget Authority by Object	29,098,845,000	28,771,241,000	(327,604,000)

[1] Reflects request to Labor/HHS/Education Subcommittee, and includes Type I Diabetes funds provided through Public Law 107–360

SALARIES AND EXPENSES

Object Classes	Fiscal year		Increase or decrease
	2007 Joint resolution	2008 estimate	
Personnel Compensation:.			
Full-Time Permanent (11.1)	$838,033,000	$881,383,000	$43,350,000
Other Than Full-Time Permanent (11.3)	263,580,000	276,142,000	12,562,000
Other Personnel Compensation (11.5)	29,783,000	31,112,000	1,329,000
Military Personnel (11.7)	26,032,000	27,721,000	1,689,000
Special Personnel Services Payments (11.8)	171,584,000	175,795,000	4,211,000
Total Personnel Compensation (11.9)	1,329,012,000	1,392,153,000	63,141,000
Civilian Personnel Benefits (12.1)	311,004,000	326,309,000	15,305,000
Military Personnel Benefits (12.2)	17,255,000	18,026,000	771,000
Benefits to Former Personnel (13.0)	.....	.....	.....
Subtotal, Pay Costs	1,657,271,000	1,736,488,000	79,217,000
Travel (21.0)	55,429,000	52,639,000	(2,790,000)
Transportation of Things (22.0)	5,174,000	4,938,000	(236,000)
Rental Payments to Others (23.2)	1,380,000	1,373,000	(7,000)
Communications, Utilities and Miscellaneous Charges (23.3)	29,949,000	29,770,000	(179,000)
Printing and Reproduction (24.0)	14,418,000	14,093,000	(325,000)
Other Contractual Services:			
Advisory and Assistance Services (25.1)	103,157,000	100,069,000	(3,088,000)
Other Services (25.2)	515,643,000	485,772,000	(29,871,000)
Purchases from Govt. Accounts (25.3)	1,177,590,000	1,146,018,000	(31,572,000)
Operation & Maintenance of Facilities (25.4)	62,671,000	62,582,000	(89,000)
Operation & Maintenance of Equipment (25.7)	76,450,000	72,506,000	(3,944,000)
Subsistence & Support of Persons (25.8)	.....	.....	.....
Subtotal Other Contractual Services	1,935,511,000	1,866,947,000	(68,564,000)
Supplies and Materials (26.0)	216,416,000	201,809,000	(14,607,000)
Subtotal, Non-Pay Costs	2,258,277,000	2,171,569,000	(86,708,000)
Total, Administrative Costs	3,915,548,000	3,908,057,000	(7,491,000)

SALARIES AND EXPENSES—TOTAL—MODIFIED DEFINITION

Institutes and centers	Fiscal year		Percent change
	2007 Joint resolution	2008 President's budget	
NCI	$312,200,000	$315,226,000	1.0
NHLBI	107,364,000	108,390,000	1.0
NIDCR	20,949,000	21,151,000	1.0
NIDDK	60,867,000	61,450,000	1.0
NINDS	54,003,000	54,561,000	1.0
NIAID	229,065,000	231,142,000	0.9
NIGMS	47,317,000	48,300,000	2.1
NICHD	57,594,000	58,425,000	1.4
NEI	22,905,000	23,098,000	.8
NIEHS	22,141,000	22,313,000	.8
NIA	37,554,000	37,942,000	1.0
NIAMS	23,537,000	23,737,000	.8
NIDCD	18,434,000	18,624,000	1.0
NIMH	73,171,000	73,901,000	1.0
NIDA	57,628,000	58,205,000	1.0
NIAAA	26,946,000	27,179,000	.9
NINR	9,367,000	9,464,000	1.0
NHGRI	18,412,000	18,581,000	.9
NCRR	27,957,000	28,235,000	1.0
NCCAM	12,698,000	12,824,000	1.0
NCMHD	10,154,000	10,260,000	1.0
NIBIB	17,155,000	17,353,000	1.2
FIC	12,582,000	12,708,000	1.0
NLM	9,875,000	9,855,000	−0.2
OD	114,136,000	107,471,000	−5.8
Clinical Center	18,248,000	18,431,000	1.0
Total	1,422,259,000	1,428,826,000	0.5
Public Health Education Excluded from above	(28,384,000)	(28,779,000)	1.4

Note.—Section 408 of the PHS Act, as amended, defines administrative expenses as expenses incurred for the support of activities relevant to the award of grants, contracts, and cooperative agreements and expenses incurred for general administration of the scientific programs and activities of the National Institutes of Health.

In collaboration with staff of the General Accounting Office (GAO), a methodology was developed to account for administrative expenses as defined in Section 408. This methodology includes obligations in the RMS budget activity (except for Program Evaluation costs), obligations directly related to the administrative responsibilities of the Office of the Scientific Director in the Intramural budget activity, and administrative expenses in the Cancer Control program.

In addition, direct program costs in the Office of the Director (those for the Director's Discretionary Fund, AIDS research, the Office of Women's Health Research, the Office of Education, the Office of Behavioral and Social Science Research, the Office of Dietary Supplements, the Loan Repayment Programs, and the Office of Rare Diseases Research) have been excluded.

The definition of administrative expenses has been further modified to include those activities specifically excluded by the law (NINR, FIC, NLM, and the Clinical Center), and to exclude public health education activities. This is consistent with previous House Appropriations subcommittee requests on administrative costs using this definition.

Major cost categories excluded from this definition but included in the OMB/HHS definition of administrative costs: salaries and benefits for researchers; travel for patients undergoing treatment at the Clinical Center and travel to scientific workshops and conferences; costs associated with laboratory facilities; contractual support for R&D activities in the Intramural program; and scientific supplies.

STATISTICAL DATA—GRANTS, DIRECT AND INDIRECT COSTS AWARDED

[Dollars in millions]

Fiscal year	Direct costs awarded	Indirect costs awarded	Total dollars awarded	Percent to total in dollars		Percent growth in dollars	
				Direct	Indirect	Direct	Indirect
1996	$6,214	$2,627	$8,840	70.3	29.7	.....	.....
1998	7,246	3,038	10,284	70.5	29.5	.....	.....
1999	8,391	3,421	11,811	71.0	29.0	15.8	12.6
2000	9,787	3,881	13,668	71.6	28.4	16.6	13.5
2001	11,210	4,425	15,634	71.7	28.3	14.5	14.0
2002	12,721	4,937	17,658	72.0	28.0	13.5	11.6
2003	14,337	5,410	19,747	72.6	27.4	12.7	9.6
2004	14,780	5,760	20,540	72.0	28.0	3.1	6.5
2005	15,299	5,915	21,214	72.1	27.9	3.5	2.7
2006	15,095	5,905	21,000	71.9	28.1	−1.3	−0.2
2007 Joint Resolution	15,290	5,982	21,272	71.9	28.1	1.3	1.3
2008 President's Budget	15,049	5,887	20,936	71.9	28.1	−1.6	−1.6

Note.—Fiscal year 2007–2008 data is preliminary, and will change as actual data is received.

RESEARCH PROJECT GRANTS—TOTAL NUMBER OF AWARDS AND DOLLARS

[Dollars in thousands]

	Fiscal year													
	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007 joint resolution	2008 revised President's budget
No. of Awards:														
Competing	6,759	6,653	7,390	7,578	8,566	8,765	9,101	9,396	10,411	10,020	9,599	9,129	10,154	9,404
Noncompeting	17,069	17,854	18,248	19,495	20,149	21,779	23,322	24,921	25,776	27,040	27,385	27,366	26,668	26,573
Subtotal (includes Non-comp)	23,828	24,507	25,638	27,073	28,715	30,544	32,423	34,317	36,187	37,060	36,984	36,495	36,822	35,977
SBIR	1,071	1,012	1,298	1,326	1,508	1,640	1,699	1,889	2,032	2,181	1,924	1,822	1,463	1,543

Total	24,899	25,519	26,936	28,399	30,223	32,184	34,122	36,206	38,219	39,241	38,908	38,317	38,285	37,520
Average Annual Cost:														
Competing	$231.2	$244.6	$245.9	$255.9	$293.6	$332.2	$333.1	$338.8	$337.8	$355.7	$354.8	$368.3	$367.5	$350.3
Total (includes noncomp)	$252.7	$262.1	$269.3	$277.7	$294.8	$319.4	$344.7	$365.5	$79.9	$392.9	$401.8	$403.2	$402.1	$402.3
Percent Change over prior year average costs:														
Competing RPGs	2.8	5.8	0.5	4.0	14.7	13.2	0.3	1.7	−0.3	5.3	−0.2	3.8	−0.2	−4.7
Total RPGs	3.8	3.7	2.7	3.1	6.2	8.4	7.9	6.0	3.9	3.4	2.3	0.4	−0.3	.....
Average Length of Award in Years	3.8	3.8	3.8	3.8	3.9	3.9	3.9	3.9	3.8	3.7	3.7	3.8	3.7	3.8

[1] As a policy, no inflationary increases were provided for competing RPGs. The apparent decrease in average cost in fiscal year 2008 is the result of an extremely large cohort of AIDS clinical trials cycling from competing into noncompeting status. (77 awards, average cost $1.8 million per award). While there will be no inflationary increases for direct, recurring costs in Noncompeting continuation RPGs, where the NIH has committed to a programmatic increase in an award, such increases will be provded.

Numbers of grants identified in fiscal year 2007 and fiscal year 2008 are estimates, and WILL change as applications are received and selected for funding.

RESEARCH PROJECT GRANTS—FISCAL YEARS 1999–2008

[Percent of success Rates]

Institutes and centers	Fiscal year									
	1999	2000	2001	2002	2003	2004	2005	2006	2007 joint resolution	2008 President's budget
NCI	32	26	27	28	27	24	20	19	19	17
NHLBI	36	35	36	33	34	29	24	20	19	18
NIDCR	24	27	34	29	27	30	24	19	20	15
NIDDK	33	28	29	34	33	27	24	21	19	17
NINDS	35	37	32	29	30	25	22	18	19	18
NIAID	34	36	38	36	35	24	25	21	22	21
NIGMS	39	37	37	39	38	30	27	26	31	25
NICHD	30	29	27	28	27	17	18	15	19	15
NEI	40	42	40	41	33	30	26	23	23	23
NIEHS	27	29	29	29	25	19	19	22	19	11
NIA	28	26	32	28	29	21	19	17	19	17
NIAMS	24	27	29	23	20	20	20	19	17	17
NIDCD	34	40	42	39	38	35	27	28	29	25
NIMH	27	29	31	28	27	24	21	20	22	19

RESEARCH PROJECT GRANTS—FISCAL YEARS 1999–2008—Continued

[Percent of success Rates]

Institutes and centers	Fiscal year									
	1999	2000	2001	2002	2003	2004	2005	2006	2007 joint resolution	2008 President's budget
NIDA	34	38	36	31	35	27	22	20	19	18
NIAAA	30	31	33	32	27	29	31	27	31	30
NINR	14	32	26	26	27	21	24	18	21	17
NHGRI	38	43	42	15	30	23	18	34	38	32
NIBIB	N/A	N/A	N/A	N/A	19	17	20	17	18	16
NCRR	34	18	29	30	28	21	14	13	21	17
NCCAM	57	29	17	14	14	17	17	14	17	21
NCMHD [1]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
FIC	39	23	30	28	19	22	24	19	20	18
ROADMAP	N/A	N/A	N/A	N/A	N/A	13	17	10	18	10
NIH	32	32	32	31	30	25	22	20	21	18

[1] NCMHD success rate is N/A due to co-funding agreements with other IC's.

Note.—Success rates identified in fiscal year 2007 and fiscal year 2008 are estimates, and WILL change as applications are received and selected for funding.

HISTORY OF OBLIGATIONS BY INSTITUTE OR CENTER [1]—FISCAL YEARS 1999–2008

[In thousands of dollars]

Institutes and centers	Fiscal year										
	1999	2000	2001	2002	2003	2004	2005	2006 actual	2006 comp.[1]	2007 revised joint resolution	2008 revised President's budget
NCI	2,918,050	3,314,580	3,758,566	4,177,830	4,595,477	4,727,365	4,797,731	4,754,121	4,795,073	4,795,491	4,782,114
NHLBI	1,788,008	2,027,286	2,298,035	2,569,794	2,793,681	2,882,601	2,922,573	2,893,527	2,915,923	2,919,980	2,925,413
NIDCR	233,605	268,521	306,152	342,292	371,630	382,013	389,346	385,589	388,664	389,370	389,722
NIDDK	1,018,063	1,167,110	1,399,184	1,560,013	1,712,959	1,829,473	1,852,592	1,838,511	1,853,149	1,855,226	1,858,045
NINDS	900,245	1,028,204	1,175,591	1,325,193	1,456,426	1,498,203	1,529,654	1,519,971	1,533,045	1,534,904	1,537,019
NIAID	1,565,201	1,777,154	2,041,311	2,339,779	3,606,789	4,141,769	4,276,433	4,274,201	4,379,199	4,366,445	4,592,482
NIGMS	1,203,079	1,366,994	1,535,056	1,722,890	1,846,917	1,915,130	1,931,690	1,916,927	1,934,043	1,935,625	1,941,462
NICHD	748,626	857,354	975,537	1,110,459	1,205,908	1,247,939	1,262,273	1,252,598	1,263,521	1,254,144	1,264,946

NEI	394,601	449,759	510,241	580,047	633,109	650,961	664,840	660,340	665,768	666,675	667,820
NIEHS	374,527	441,960	501,813	574,518	614,183	630,254	640,405	630,447	635,995	641,773	637,406
NIA	594,556	685,695	785,413	891,282	993,595	1,021,376	1,045,339	1,036,559	1,045,201	1,046,500	1,047,148
NIAMS	307,160	349,555	396,305	447,682	486,031	499,368	507,843	502,954	507,416	508,060	508,082
NIDCD	229,162	263,448	300,282	341,260	370,330	380,737	391,679	389,623	393,111	393,540	393,682
NIMH	858,520	972,127	1,106,095	1,245,292	1,341,014	1,379,225	1,403,007	1,390,009	1,401,813	1,403,570	1,405,421
NIDA	611,061	694,561	790,185	892,639	965,721	991,510	1,000,056	990,405	998,858	1,000,014	1,000,365
NIAAA	258,874	291,928	340,151	383,174	415,960	427,223	435,503	431,726	435,479	436,057	436,505
NINR	69,600	89,415	104,294	120,217	130,537	134,279	137,199	136,020	137,150	137,287	137,800
NHGRI	279,030	335,129	381,971	428,248	464,960	490,546	485,500	481,339	485,655	486,427	484,436
NIBIB	.....	.....	.....	111,740	278,279	286,684	296,324	293,954	298,088	298,391	300,463
NCRR	562,082	676,077	817,098	1,010,169	1,138,820	1,191,556	1,108,028	1,088,500	1,108,947	1,143,841	1,112,498
NCCAM	40,464	77,808	89,120	104,334	113,405	116,590	121,333	120,294	121,134	121,379	121,699
NCMHD	.....	.....	130,070	157,364	185,674	190,824	194,904	193,522	195,263	199,429	194,495
FIC	35,307	43,446	50,430	56,787	63,425	65,160	66,164	65,726	66,317	66,422	66,594
NLM	181,014	213,730	239,068	275,395	299,771	310,165	312,980	311,721	314,078	320,229	312,562
OD	255,584	281,587	212,482	234,784	266,161	327,267	533,673	724,831	478,307	1,096,985	517,062
Subtotal	15,426,419	17,673,428	20,244,450	23,003,182	26,350,762	27,718,218	28,307,069	28,283,415	28,351,197	29,017,764	28,635,241
B&F	216,856	140,311	205,756	114,839	305,628	303,254	239,246	170,456	85,505	81,081	136,000
TOTAL	15,643,275	17,813,739	20,450,206	23,118,021	26,656,390	28,021,472	28,546,315	28,453,871	28,436,702	29,098,845	28,771,241
Interior/Superfund	.....	.....	62,850	70,212	83,515	78,300	79,836	79,108	79,108	79,117	78,434
Total, Budget Authority	15,643,275	17,813,739	20,513,056	23,188,233	26,739,905	28,099,772	28,626,151	28,532,979	28,515,810	29,177,962	28,849,675

[1] Obligations for actual years exclude lapse. Includes funds for Type I Diabetes Initiative.
[2] Fiscal year 2006—Comparable includes all comparable adjustments.

HISTORY OF OBLIGATIONS BY TOTAL MECHANISM [1]—FISCAL YEARS 1999–2008

[In thousands of dollars]

Budget mechanism	Fiscal year										
	1999	2000	2001	2002	2003	2004	2005	2006 actual [2]	2006 comp.[3]	2007 revised joint resolution	2008 revised President's budget
Res. Project Grants	8,779,019	10,118,249	11,557,511	12,995,051	14,239,043	15,165,836	15,426,097	15,313,663	15,332,997	15,417,256	15,080,819
Research Centers	1,380,117	1,547,152	1,859,600	2,123,723	2,425,448	2,545,972	2,647,355	2,659,653	2,804,893	2,895,051	2,917,412
Other Research	808,100	1,013,499	1,218,906	1,450,750	1,587,841	1,651,823	1,655,743	1,650,974	1,669,351	1,767,797	1,747,167

HISTORY OF OBLIGATIONS BY TOTAL MECHANISM [1]—FISCAL YEARS 1999–2008—Continued

[In thousands of dollars]

Budget mechanism	Fiscal year										
	1999	2000	2001	2002	2003	2004	2005	2006 actual [2]	2006 comp. [3]	2007 revised joint resolution	2008 revised President's budget
Subtotal Res. Grants	10,967,236	12,678,900	14,636,017	16,569,524	18,252,332	19,363,631	19,729,195	19,624,290	19,807,241	20,080,104	19,745,398
Research Training	509,185	539,510	589,624	650,686	711,441	740,506	743,861	731,121	748,641	771,600	769,413
R & D Contracts	1,067,197	1,147,672	1,387,989	1,642,046	2,299,140	2,691,897	2,516,611	2,582,606	2,667,066	2,783,528	2,975,285
Intramural Research	1,564,547	1,746,220	1,950,859	2,225,292	2,564,664	2,658,853	2,737,865	2,745,676	2,772,036	2,791,706	2,774,311
Res. Mgt. & Support	542,188	600,203	690,929	786,647	927,297	977,771	1,014,754	1,098,953	1,108,615	1,132,127	1,142,492
Cancer Control	306,734	389,425	459,482	501,208	533,173	529,980	531,634	505,705	505,705	516,565	516,565
Construction	32,734	76,181	78,000	117,600	496,782	118,148	178,560	29,700	29,700	.....	.....
Library of Medicine	181,014	213,730	239,068	275,395	299,771	310,165	312,980	311,721	311,264	320,229	308,415
Office of the Director	255,584	281,587	212,482	234,784	266,161	327,267	533,673	724,831	393,009	613,985	395,522
Subtotal	15,426,419	17,673,428	20,244,450	23,003,182	26,350,761	27,718,218	28,299,133	28,354,603	28,343,277	29,009,844	28,627,401
Buildings & Facilities	216,856	140,311	205,756	114,839	305,628	303,254	247,182	178,376	93,425	89,001	143,840
Total	15,643,275	17,813,739	20,450,206	23,118,021	26,656,389	28,021,472	28,546,315	28,532,979	28,436,702	29,098,845	28,771,241
Interior—Superfund	62,850	70,212	83,515	78,300	79,836	79,108	79,108	79,117	78,434		
Total Budget Authority	15,643,275	17,813,739	20,513,056	23,188,233	26,739,904	28,099,772	28,626,151	28,532,979	28,515,810	29,177,962	28,849,675

[1] Obligations for actual years exclude lapse.
[2] Fiscal year 2006 Actual Obligations include Interior (previously VA/HUD) Superfund activities within the Mechanism amounts.
[3] Fiscal year 2006 Comparable includes all transfers and comparable adjustments.
[4] B&F Budget Mechanism includes the B&F appropriation plus the following included in NCI: Fiscal year 2005—$7,936,000; fiscal year 2006—$7,920,000; fiscal year 2007 (est.)—$7,920,000; fiscal year 2008 (est)—$7,840,000.

Note.—All amounts include funds for Type I Diabetes Initiative.

OPASI

Question. I understand that you envision a significant role for the Office of Portfolio Analysis and Strategic Initiatives in future NIH activities. At present, the Office has a relatively small dedicated budget and workforce. Please provide us with an updated mechanism table for OPASI showing the enacted fiscal year 2007 enacted level and the fiscal year 2008 President's budget request. Please also provide narrative regarding your vision for OPASI's future role at NIH including, but not limited to, the following: The activities you envision OPASI performing.

Answer. The Office of Portfolio Analysis and Strategic Initiatives (OPASI) is a policy office within the NIH Office of the Director. Related grant-making activities are carried out within the Common Fund/Roadmap.

The goal of the Office is to support the ICs in their collaborative efforts. OPASI accomplishes its mission through the efforts of three Divisions: the Division of Resource Development and Analysis, the Division of Strategic Coordination, and the Division of Evaluation and Systemic Assessments. These divisions work together to analyze the existing NIH research portfolio, collaborate with the ICs to plan and manage new research initiatives via the Common Fund, and provide evaluation support to the ICs so that future programs can be improved. The NIH has also established a Council of Councils (CoC) to give advice on OPASI activities. The CoC is composed of scientific and lay council members from the IC Advisory Councils and the NIH Council of Public Representatives who simultaneously serve on the CoC and their home councils.

Division of Resource Development and Analysis: This Division develops tools, analyses, and resources that can be used within OPASI and in the ICs to monitor and report on spending in specific areas; performs portfolio analyses, particularly with respect to a wide variety of scientific areas in which multiple ICs are active; collects, distributes, and analyzes data on public health burden of disease as well as the impact of research on disease burden. One portfolio analysis tool being developed by this division, is the RCDC (Research, Condition and Disease Categorization system, formerly known as the Knowledge Management and Disease Coding system, KMDC) This system is a state of the art reporting tool that streamlines the process of identifying grants, contracts, and intramural research projects that are relevant to particular diseases, conditions, or scientific topics. The tool will first be used for category reporting for the fiscal year 2010 budget.

The RCDC use as a portfolio analysis tool for planning purposes will expand beyond OPASI to the ICs in fiscal year 2008 as personnel are trained in the use of the system.

Division of Strategic Coordination.—This Division works closely with the ICs to manage the Common Fund, which funds the NIH Roadmap. Since many cross-cutting areas are funded through IC collaborations outside the context of the Common Fund, special criteria have been established for Common Fund initiatives. OPASI staff in this Division work closely with ICs to gather ideas for possible Common Fund initiatives, to determine the responsiveness of these ideas to the Common Fund/Roadmap criteria, and to prioritize the ideas based in part on analysis of current funding in these areas using tools from the Division of Resource Development and Analysis. Those areas not selected for Roadmap emphasis may be addressed through multi-IC collaborations outside the scope of OPASI management. Staff in this Division will also increasingly be involved in post-award management of Common Fund initiatives, reviewing progress of individual projects as well as providing an overall assessment of whether program goals and milestones are being met.

Division of Evaluation and Systemic Assessments.—This Division manages the NIH portion of the PHS Evaluation Set-Aside funds and works with ICs to develop evaluation plans for their programs. In addition, the Division provides expertise for the evaluation of multi-IC-supported programs, including those that are supported via the Common Fund. This activity will expand in future years to include an In-House studies team that will conduct evaluations of Common Fund/Roadmap and other trans-NIH programs. This Division also manages the coordinated development and submission of Systemic Assessment documents in response to the Government Performance Results Act (GPRA) and the Office of Management and Budget's Performance Assessment Rating Tool (PART).

Question. Any grant-making or grant-administering activities you envision OPASI performing?

Answer. A fundamental tenet of the Common Fund is that the initiatives should benefit and synergize with the missions of multiple or all ICs. The management of Common Fund initiatives is therefore inherently of interest to the ICs and is best served by highly engaged scientific program staff working in the ICs. For this reason, the grant-making authority and much of the grant administration of Common

Fund initiatives lies in the ICs. However, IC staff work on individual initiatives that are of particular interest to their IC and therefore may not maintain perspective on the program as a whole. The role of OPASI throughout the process of Common Fund management is to provide an over-arching view and perspective of the Common Fund and the scientific goals that all of the initiatives are expected to meet. OPASI staff work on teams that consist primarily of IC staff to plan each of the initiatives, to review progress, to develop specific budgetary plans, and to develop evaluations for individual initiatives; their participation in all of the teams provides an over-arching central level of management that insures that the trans-NIH nature of the initiatives is maintained.

In addition to the Common Fund, OPASI oversees funding available to NIH from the PHS Evaluation Set-Aside. These funds are administered and managed by the Division of Evaluation and Systemic Assessment. The Division assesses funding requests from ICs for technical and conceptual merit as well as policy relevance. This is an internal process designed to ensure high quality program evaluations rather than a grant-making authority.

Question. Broad strokes estimates for future growth of the office in terms of FTE's and budget (not including amounts appropriated separately for the Common Fund).

Answer. OPASI future growth will occur in all three Divisions. Recruitment is underway in the Division of Strategic Coordination to allow central scientific staff involvement in all of the Common Fund initiatives. The current staffing level will be re-evaluated in fiscal year 2008 after the second cohort of initiatives is funded and while a third cohort is being planned to determine whether additional staff are needed in fiscal year 2009 and beyond. The Division of Resource Development and Analysis is expected to grow in fiscal year 2008 to accommodate increased portfolio analysis and planning both within OPASI and in the ICs. Its growth beyond fiscal year 2008 will involve the recruitment of staff to develop new tools to enhance the ability to plan for, assess, and manage complex portfolios and to expand the capacity to analyze Public Health Burden. The Division of Evaluation and Systemic Assessment will expand in fiscal year 2008 to increase the capability of doing evaluations in-house. FTEs are expected to grow consistent with the funds available for OPASI, currently funded at $7,826,000 (includes one-time funding of $4,550,000 for Research, Condition and Disease Categorization) in fiscal year 2007 to $4,450,000 in fiscal year 2008, a decrease of $3,376,000 over fiscal year 2007.

QUESTION SUBMITTED BY SENATOR DANIEL K. INOUYE

BEHAVIORAL RESEARCH

Question. Every year since fiscal year 1999, this Subcommittee has urged the NIH to support basic behavioral research and to find an organizational home for this activity. Basic research is the building block for subsequent discoveries that lead to improved treatments and cures. This, of course, is also true for behavioral research. How do you intend to ensure dedicated scientific leadership for basic behavioral research at the NIH?

Answer. Basic behavioral and social sciences research (BSSR) is critical to the NIH mission and the Agency will continue to support work in these disciplines. We estimate that NIH support for basic BSSR has been over $1.0 billion annually since fiscal year 2004. NIA, NIDA, NICHD, NIMH and NIAAA have provided particularly strong funding in this area.

The Office of Behavioral and Social Sciences Research (OBSSR), located within the Office of the Director, is key to leading, coordinating and participating in NIH BSSR activities, including basic BSSR. OBSSR participates in funding opportunity announcements developed by individual or small groups of Institutes and Centers (ICs) and also leads in the development of such initiatives. However, OBSSR does not fund initiatives directly or entirely and is dependent on individual ICs for support and funding of specific programs. The Office participates in the Genes, Environment and Health Initiative, the NIH Blueprint for Neuroscience Research, and the NIH Roadmap for Medical Research. It has taken the lead on several Roadmap initiatives, including RFA RM 07-004, Facilitating Interdisciplinary Research via Methodological and Technological Innovation in the Behavioral and Social Sciences (R21) (http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-004.html). Slated for funding in fiscal year 2007, this initiative seeks to foster better integration of the behavioral and social sciences with biomedical research with the ultimate goal of improving health.

Under the leadership of its Director, Dr. David Abrams, OBSSR has recently completed a two-year strategic planning process that identified four major pro-

grammatic directions for the Office. As articulated in the Strategic Prospectus (http://www.conceptsystems.com/OBSSR/OBSSR-Prospectus-final.pdf), the first programmatic direction is "next generation" basic BSSR that will be informed by breakthroughs in complementary areas such as genetics, informatics, and multilevel analyses. Specific priority areas include but are not limited to the following:

—*Gene-Environment interactions*.—How are genetic traits and early life experiences linked to physical and emotional health later in life?

—*Biosocial stress markers*.—What are the biological sequelae of stress, and how do they relate to long-term mental and physical health?

—*Technology, Measurement and Methodology*.—How can we improve biomarker, behavioral and environmental data collection to better understand pathways linking biology, behavior, environment, and society?

—*Spirituality and health*.—How do individual belief systems or social religious norms affect health?

—*Work-related stresses*.—How are conflicts between work and family associated with social stress and health?

—*Social integration and social capital*.—How have advances in technology and mobility affected neighborhood social networks, health behaviors and health outcomes?

—*Inequality and health outcomes*.—How do large-scale societal structures (e.g., racial segregation, immigration and acculturation patterns, socioeconomic status) impact health?

As a first step in the realization of "next generation" basic BSSR, OBSSR is currently leading a partnership among several ICs and the Centers for Disease Control and Prevention to issue new funding opportunity announcements to support behavioral and social science research on understanding and reducing health disparities (see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-063.html). The Office is also working with IC partners on activities to support research on gene-social environment interactions and in fiscal year 2008 plans to sponsor a summer institute to train behavioral and social scientists in genetics/genomics.

The senior leadership at NIH believes that the current NIH-wide approach of having basic BSSR within and across many ICs, and having OBSSR play a coordinating or leadership role, is the optimal arrangement for this area of research. Moreover, the NIH Reform Act of 2006 established the new Division of Program Coordination, Planning, and Strategic Initiatives, of which OBSSR will be a part. This change will enhance OBSSR's coordinating and leadership roles, working in the new Division and with ICs to ensure the support of the highest quality basic and applied BSSR throughout the NIH.

SUBCOMMITTEE RECESS

Senator HARKIN. So, thank you all for being here. The subcommittee will stand in recess to reconvene at 3:30 p.m., Monday, March 26, in room SD–116.

[Whereupon, at 3:05 p.m., Monday, March 19, the subcommittee was recessed, to reconvene at 3:30 p.m. Monday, March 26.]