Statement for hearing entitled, “NIH in the 21st Century: The Director’s Perspective”

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Good morning, Mr. Chairman and distinguished Members of the Subcommittee:

It is an honor to appear before you today to discuss the state of the National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services (HHS), and my vision for the future of biomedical research.

First, I’d like to thank this Subcommittee for its steadfast support of NIH’s mission: discovering fundamental knowledge about living systems and then applying that knowledge to fight illness, reduce disability, and extend healthy life. NIH is grateful for the confidence that Congress has in our ability to advance this mission. I had the privilege to appear before this Committee in the past as Director of the National Human Genome Research Institute, and I appreciated the opportunity to contribute to your pivotal work on the landmark Genetic Information Nondiscrimination Act. Now, as steward of NIH’s entire research portfolio, I look forward to working together with you to explore the frontiers of biomedical research to improve America’s health.

I returned to NIH as Director in August of last year, and am extremely proud to stand at the helm of the most significant institution supporting biomedical research in the world. Begun as a one-room Laboratory of Hygiene in 1887, the National Institutes of Health (NIH) today has grown into a complex and multidisciplinary engine for discovery and innovation, comprised of 27 different Institutes and Centers. More than four-fifths of the NIH budget is devoted to funding competitive grants that support more than 325,000 research personnel at more than 3,000 institutions, which are located in all 50 states, the territories, and more than 90 countries around the world. More than 130 researchers funded by NIH have gone on to win Nobel Prizes.

NIH funds research only after the completion of a two-tiered review process, which is considered the “gold standard” of scientific review. Peer review panels comprising external experts evaluate the scientific merit of grant applications and then
Institute advisory councils consider how well the applications address the Institute’s mission and programmatic priorities. The process is highly rigorous and competitive; currently, about one application in five is funded.

One of my first actions upon being named NIH Director was to scan this vast landscape of biomedical research for areas ripe for major advances that could yield substantial benefits in coming years. I found many of the most exciting opportunities could be grouped under five main themes: taking greater advantage of high-throughput technologies; accelerating translational science, that is, turning discovery into health; helping to reinvent health care; focusing more on global health; and reinvigorating the biomedical research community. With Congress’ support, we are poised to take greater advantage of these unprecedented opportunities, all with the aim of helping people live longer, healthier, and more rewarding lives.

THE RESEARCH MARATHON: HOW FAR WE’VE COME

Our nation’s biomedical research effort is in a race that we cannot afford to lose. Science is not a 100-yard dash. It is a marathon – a marathon run by a relay team that includes researchers, patients, industry experts, lawmakers, and the public. Thanks to discoveries funded through NIH appropriations, we have covered a lot of distance in this marathon. Let us take a moment to look back at a few of the advances made possible by NIH-supported research, and then look ahead to some of our nation’s biggest health challenges and how NIH intends to meet them.

U.S. life expectancy has increased dramatically over the past century and still continues to improve, gaining about one year of longevity every six years since 1990. A
baby born today can look forward to an average life span of nearly 78 years, almost three decades longer than a baby born in 1900.\textsuperscript{1,2}

Not only are people living longer, they are staying active longer. From 1982 through 2005, the proportion of older people with chronic disabilities dropped by almost a third, from 27\% to 19\%.\textsuperscript{3}

We have made some of the most impressive gains against cardiovascular disease. In the mid-20\textsuperscript{th} century, cardiovascular disease caused half of U.S. deaths, claiming the lives of many people still in their 50s or 60s.\textsuperscript{4} Today, the death rate for coronary heart disease is more than 60\% lower -- and the death rate for stroke, 70\% lower – than in the World War II era.\textsuperscript{5,6}

What prompted these improvements? One major contributor has been the insights from the NIH-funded Framingham Heart Study, which began in the late 1940s and is still going strong. This population-based study, which changed the course of public health by identifying key risk factors for heart disease, will break new ground with the recent addition of detailed genetic analyses to the research project.


\textsuperscript{6} NHLBI Morbidity and Mortality: 2009 Chart Book on Cardiovascular, Lung, and Blood Diseases, page 23.
NIH-supported research also led to minimally invasive techniques to prevent heart attacks and to highly effective drugs to lower cholesterol, control high blood pressure, and break up artery-clogging blood clots. NIH-funded science has also helped people make lifestyle changes that promote health, such as eating less fat, exercising more, and quitting smoking.

Many chronic conditions begin as part of the aging process. One such disease, osteoporosis, can result in life-threatening bone fractures among older people. NIH-funded research has led to new medications and management strategies for osteoporosis that have reduced the hospitalization rate for hip fractures by 16% since 1993.\textsuperscript{7} Science has also transformed the outlook for people with age-related macular degeneration, a major cause of vision loss among the elderly. Twenty years ago, we could do little to prevent or treat this disorder. Today, because of new treatments and procedures based in part on NIH research, 1.3 million Americans at risk for severe vision loss over the next five years now can receive potentially sight-saving therapies.\textsuperscript{8}

Biomedical research also has benefitted those at the beginning of life. NIH-funded research has given hearing to thousands of children who were born profoundly deaf. Their hearing is made possible with a cochlear implant, an electronic device that mimics the function of cells in the inner ear. Since HHS’s Food and Drug Administration (FDA) approved cochlear implants for pediatric use in 2000, more than 25,000 children have received the devices, enabling many to develop normal language skills and succeed in mainstream classrooms.\textsuperscript{9}

\textsuperscript{7} Fatalities and Injuries from Falls Among Older Adults --- United States, 1993--2003 and 2001--2005. \textit{MMWR}. 2006;55(45);1221-1224.


Then, there are the infectious diseases – diseases that respect no boundaries in today’s globalized economy or when it comes to age, sex, or physical fitness. One of NIH’s greatest achievements over the past 30 years has been to lead the global research effort against the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) pandemic. Building discovery upon discovery, researchers first achieved fundamental insights about how HIV works, and then went on to develop rapid HIV tests, identify a new class of HIV-fighting drugs, and, ultimately, figure out how to combine those drugs in life-saving ways. While the battle against HIV/AIDS continues, today, HIV-infected people in their 20s who receive combination therapy may expect to live to age 70 or beyond.  

CONTINUING THE RACE: HOW FAR WE HAVE TO GO

Although we have accomplished much, the opportunities for advancing human health that we see in front of us have never been greater.

Consider the challenges posed by cancer. This disease still claims the lives of more than 500,000 Americans annually – about one every minute.  

But in 2007, for the first time in our nation’s history, the absolute number of cancer deaths in the U.S. went down. And, over the past 15 years, cancer death rates have dropped 11.4% among women and 19.2% among men, which translates into some 650,000 lives saved – more than the population of Washington, D.C. Such progress is even more striking when one considers that many cancers are strongly associated with aging, and that the U.S. population is growing increasingly older. These are encouraging milestones, but they are not nearly enough.

12 McCarthy, M. Number of Cancer Deaths Continue to Fall in the United States. Lancet 2007;369: 263.
13 American Cancer Society. Cancer Death Rates Steadily Declining.. Available at: http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Cancer_Death_Rate_Steadily_Declining.asp.
NIH-funded research has revolutionized how we think about cancer. A decade or two ago, cancer treatment was mostly reactive; diagnosis was based on the organ involved and treatment depended on brute force therapies that were highly toxic and often greatly diminished the patient’s quality of life. Today, basic research in cancer biology is moving treatment toward more effective, targeted, and less toxic therapies tailored to the genetic profile of each patient – and each patient’s cancer.

Among the early success stories in this area is the drug trastuzumab (Herceptin) for breast cancer. An NIH-sponsored clinical trial studied the effectiveness of trastuzumab combined with standard chemotherapy in reducing recurrence of the disease. The trial found that breast cancer patients whose tumors have certain genetic markers indicating a responsiveness to trastuzumab reduced their risk of cancer recurrence by 52%.\textsuperscript{14} That improvement is the best ever reported in post-surgical treatment of breast cancer. Studies also have found that the chemotherapy drugs gefitinib (Iressa) and erlotinib (Tarceva) work much better in the subset of lung cancer patients whose tumors have a certain genetic signature.\textsuperscript{15,16}

To accelerate the development of more individualized strategies for more types of cancer, NIH has tapped into the promise of high-throughput technologies and launched The Cancer Genome Atlas (TCGA). Over the next few years, TCGA’s research team will build comprehensive catalogs of the key genomic changes in 20 major types and subtypes of cancer. These data are being shared rapidly with the worldwide scientific community, and will provide powerful new guides for all those striving to develop better ways to diagnose, treat, and prevent cancer.


Already, TCGA has produced a comprehensive molecular classification system for ovarian cancer and glioblastoma, which is the most common form of brain cancer. Our survey of glioblastoma recently revealed five new molecular subtypes of the disease. In addition, researchers found that responses to aggressive therapies for glioblastoma varied by subtype. These findings hold the promise that we can match the most appropriate therapies to individual brain cancer patients and may also lead to therapies directed at the molecular changes underlying each subtype, as we are already able to do for some types of breast cancer.

Diabetes is another disease that is devastating our nation’s health. More than 23 million Americans currently have diabetes – nearly 8% of the population. Another 57 million adults have blood sugar levels that indicate they are at serious risk of developing the disease, which is a major cause of kidney failure, stroke, heart disease, lower-limb amputations, and blindness.

For type 2 diabetes, prevention appears to be the name of the game. This form of the disease, which accounts for more than 90% of cases, often can be averted or delayed


21 Cowie, 1264-1265.


23 U.S. Census Bureau, resident population estimates for 11/1/2007.
by lifestyle changes.\textsuperscript{24} The NIH-funded Diabetes Prevention Program (DPP) trial showed that one the most effective ways to lower the risk of type 2 diabetes is through regular exercise and modest weight loss.\textsuperscript{25} There is good reason to believe that such efforts may lead to a lifetime of additional health benefits. A recent follow-up study of DPP participants found the protective effects of weight loss and exercise persist for at least a decade.\textsuperscript{26} NIH also led research efforts to explore ways to implement DPP findings in real-world settings at lower cost, such as in YMCAs. The United Health Group has recently announced a partnership with YMCAs and Walgreen’s pharmacies to implement on a national scale what we have learned from this groundbreaking NIH-funded research.

More than one-third of adults in the U.S. are obese, according to the latest data from the National Health and Nutrition Examination Survey, which is conducted by the Centers for Disease Control and Prevention (CDC).\textsuperscript{27} And there are troubling signs that the next generation may face an even greater struggle. Over the past 30 years, obesity has more than doubled among U.S. children aged 2 through 5 and nearly tripled among young people over the age of 6.\textsuperscript{28,29} These statistics mean that tens of millions of Americans face an increased risk of type 2 diabetes, as well as cardiovascular disease, high blood pressure, certain cancers, osteoarthritis, and other serious health problems associated with excess body fat.


\textsuperscript{29} Health E-Stat, June 2010. Available at: http://www.cdc.gov/nchs/data/hestat/obesity_child_07_08/obesity_child_07_08.htm,
To fight America’s obesity epidemic, NIH has launched a variety of initiatives aimed at developing innovative approaches for weight control. One such effort, called the National Collaborative on Childhood Obesity Research, has pulled together experts from four NIH Institutes, the CDC, and the Robert Wood Johnson Foundation. An example of their work is the Trial of Activity for Adolescent Girls, a national study to develop and test school- and community-based interventions to get girls more involved in gym class, organized sports, or recreational activities. Another NIH program, called We Can!, provides families with practical tools for weight control at more than 1,000 community sites nationwide.

Meanwhile, other NIH-funded researchers are busy uncovering information about genes and environment that might point the way toward more personalized, targeted strategies for controlling weight and preventing diabetes. For example, in just the past few years, we have identified more than 30 genetic risk factors for type 2 diabetes.

Uncovering possible genetic factors may also help address the urgent demographic reality of Alzheimer’s disease (AD). In the United States, it is estimated that as many as 5.1 million people may have Alzheimer’s, and by 2050, with the aging of the baby boomers, that number could double. In a relentless search to find ways to slow down or prevent AD, the NIH is employing a variety of new technologies and approaches to identify genes that may play a role in risk of late-onset Alzheimer’s. Through various clinical, neuroimaging, genetic, and fluid biomarker measures to assess the sequence of events in the brain which leads from normal cognition to AD, a public-private partnership called the AD Neuroimaging Initiative is showing some success in finding methods for early diagnosis and assessing whether drugs and other interventions can prevent or delay the onset of AD. Since 2006, NIH has funded close to 60 AD translational research projects that support early drug discovery and preclinical drug development for AD and age-related cognitive decline.

A better understanding of genetic and environmental factors may help solve a frustrating medical puzzle: the causes of autism. Children with autism spectrum disorders experience a range of problems with language and social interactions, sometimes accompanied by repetitive behaviors or narrow, obsessive interests. Recent studies funded by NIH have associated autism risk with several genes involved in the formation and maintenance of brain cells, but much more work is needed to follow these clues.

Now and in coming years, NIH will support comprehensive and innovative approaches to piece together the complex factors that contribute to autism spectrum disorders. One ambitious effort will involve sequencing the complete genomes of 300 people with autism and their parents. Other researchers will examine mothers’ exposures during pregnancy to identify possible environmental factors. NIH hopes to use these insights to develop new molecular and behavioral therapies for such disorders, as well as identify possible strategies for prevention.

Another brain disorder, depression, presents a different set of challenges. Although researchers have made significant progress in understanding the biology of depression, improving treatment, and lessening the social stigma associated with mental illnesses, suicide is the fourth leading cause of death among young people between the ages of 15 and 24. Untreated depression can also reduce productivity, cause family stresses, and increase the risk for serious health problems, such as substance abuse and heart disease.

How can medical research reduce depression’s tragic toll? One way is to recognize that this is a brain disease, and to seek out its molecular underpinnings. Researchers today are using functional magnetic resonance imaging and other innovative technologies to see how the brains of people with depression differ from those without the disorder. Another critical need is optimizing therapy. Finding the

right antidepressant drug for any particular patient currently is a lengthy, trial-and-error process that can take weeks or months before symptoms are relieved. NIH supports laboratory research aimed at developing quicker-acting antidepressants, as well as genetic studies that will help to match individuals with the drugs most likely to work for them.

In 2009, 160 U.S. active-duty soldiers committed suicide – the highest level since the Army began keeping records three decades ago. To address and prevent these tragedies, NIH and the U.S. Army recently partnered to launch the largest study ever of suicide and mental health among military personnel. The Army Study to Assess Risk and Resilience in Service Members (Army STARRS) will identify risk factors that may enable us to develop more effective approaches to suicide prevention.

TRANSFORMING DISCOVERY INTO HEALTH

Whatever the disease, be it depression, diabetes, or something much rarer, NIH’s emphasis today and beyond will be on translating basic discoveries into new diagnostic and treatment advances in the clinic.

Of course, that kind of translation must be built upon a vigorous foundation of basic science research supported by NIH – or else there will be nothing to translate. A few decades ago, when researchers began studying a rare hereditary disorder that resulted in very high cholesterol levels, some might have argued that this basic investigation of lipid metabolism was rather obscure and irrelevant to the medical care of most of the population. But out of that research came the understanding of how cholesterol is synthesized in the liver, and a direct consequence was the development of a class of drugs, known as statins, which has saved countless lives from heart disease.

Today, there are unprecedented discoveries coming from basic research that have been made possible by the emergence of fields such as genomics, and technological advances such as high throughput technologies. These opportunities will ultimately lead to breakthroughs in our understanding of the causes of many diseases and to new targets and pathways for potential treatments. What makes these opportunities so extraordinary is that they enable us to take a much more comprehensive approach to human biology. Now, we can focus on *all* of the genes, proteins, and pathways in a molecular and cellular network, enabling a thorough elucidation and understanding of their roles in multiple disease processes.

For many disorders, these new insights into molecular mechanisms represent new opportunities for NIH to shorten and straighten the pathway from discovery to health. This expectation is grounded in several recent developments: the dramatic acceleration of our basic understanding of hundreds of diseases; the establishment of NIH-supported centers that enable academic researchers to use such understanding to screen thousands of chemicals for potential drug candidates; and the emergence of public-private partnerships to aid the movement of drug candidates identified by academic researchers into the commercial development pipeline.

Let me give you one exciting example of how NIH will implement this strategy: the Therapeutics for Rare and Neglected Diseases (TRND) program. This effort will bridge the wide gap in time and resources that often exists between basic research discoveries and the human testing of new drugs.

A rare disease is one that affects fewer than 200,000 Americans. However, if all 6,800 rare diseases are considered together, they afflict more than 25 million Americans. Private companies seldom pursue new therapies for these types of diseases because of the high cost of research and low likelihood of recovering their investments. Effective drugs exist for only about 200, or less than 3%, of these rare diseases. But not all neglected diseases are rare. Some of these diseases affect hundreds of millions of people who live in low income countries, but, because of lack of economic incentives,
there is a dire shortage of effective, affordable treatments for these major global causes of death and disability.

Working in an open environment in which all of the world’s top experts on a disease can be involved, TRND will enable certain promising compounds to be taken through the preclinical development phase – a time-consuming, high-risk phase often referred to as “the valley of death” by pharmaceutical firms focused on the bottom line. Besides speeding development of drugs for rare and neglected diseases, TRND will serve as a model for therapeutic development for common diseases, many of which are being resolved into smaller, molecularly distinct subtypes.

NIH is taking other steps to re-engineer the pipeline that connects all of the points between the identification of a potential therapeutic target by a basic researcher and FDA approval of a therapeutic for clinical use. Among our new tools is the NIH Clinical and Translational Sciences Award program, which currently funds 46 centers in 26 states, and will add more this year. This national network is pulling together interdisciplinary clinical research teams to work in unprecedented ways to develop and deliver tangible health benefits. Another powerful resource for translation is the nation’s largest research hospital, the Mark O. Hatfield Clinical Research Center, located on the NIH campus in Bethesda, MD. Just as they blazed a trail for safe and effective human gene therapy, NIH clinical researchers may be well positioned to discover other pioneering approaches to human therapeutics, such as those using human embryonic stem cells or induced pluripotent stem cells derived from skin cells.

To make the most of these new opportunities, the NIH and FDA recently forged a landmark partnership with the formation of a Joint Leadership Council. Members of this Leadership Council will work together to ensure that regulatory considerations form an integral component of biomedical research planning, and that the latest science is integrated into the regulatory review process. Such collaboration will advance the development of products to treat, diagnose and prevent disease, as well as enhance the safety, quality, and efficiency of clinical research and medical product approval.
NIH REFORM ACT

The NIH Reform Act of 2006, which was conceptualized, crafted, and codified through the efforts of this Subcommittee during the 109th Congress, provided NIH with two key tools for optimizing the use of scientific and funding resources. We have fully implemented this landmark legislation, and I would like to provide you with an update on two of these key features: The Common Fund and the Scientific Management Review Board.

The Common Fund fosters collaboration and interdisciplinary research, allowing NIH to bring the best minds together to solve the most complex problems and stimulate innovation. For example, The Common Fund’s Molecular Libraries program gives academic researchers access to large-scale screening capacity similar to that found at publicly funded, mid-sized pharmaceutical companies, empowering them to move their research beyond basic discoveries into the early components of the drug development pipeline. More than 100 promising new compounds have already been identified through this program.

Another large-scale effort funded through the Common Fund, the Human Microbiome Project, several weeks ago published its analysis of the genomes of 178 types of microbes that live in or on the human body.33 The researchers discovered novel genes in these microbes, adding a new level of understanding to what we know about these microorganisms and how they contribute to human health and disease.

By authorizing the NIH Common Fund, this Subcommittee underscored NIH’s need for flexibility to plan and adjust research priorities based on public health needs and scientific opportunities. The Subcommittee also recognized that some of the most promising new approaches to biomedical research have potential applications to multiple diseases and organ systems, and, therefore, can be difficult to fund through the usual priority-setting processes of the 27 Institutes and Centers. The Common Fund has

33 Science 21 May 2010 Vol. 328. no.5981, pp. 994-999
provided an exciting and powerful new source of “venture capital” for such crosscutting and innovative initiatives.

The NIH Reform Act also created a key advisory committee, the Scientific Management Review Board (SMRB), through which outside experts provide advice to the NIH Director on the organizational structure of NIH, with a specific focus on whether modifications to the structure are needed to optimize the management of scientific funds and resources. The SMRB is currently addressing organizational questions related to the management of research on substance use, abuse, and addiction and carrying out a comprehensive review of the role and structure of the NIH intramural program, including the Clinical Center. The Board has also developed a framework for considering organizational change, which will be used to guide its work.

BIOMEDICAL RESEARCH PROPELS U.S. ECONOMY

Investing in NIH not only improves America’s health and strengthens our nation’s biomedical research potential, it propels the U.S. economy. Consider the following statistics:

- A report issued by Families USA estimated that in 2007, every $1 in NIH funding resulted in an additional $2.11 in economic output in the U.S.\(^\text{34}\)
- In FY 2007, a typical NIH grant supported the salaries of about 7 primarily high-tech jobs in full or in part.\(^\text{35}\) The 351,000 jobs resulting from NIH awards paid an average annual wage of more than $52,000 per annum and account for more than $18 billion in wages for FY 2007.\(^\text{36}\)


\(^{36}\) FamiliesUSA (2008). In Your Own Backyard.
• Long term, NIH funded R&D sparks U.S. economic innovation in the high-technology and high value-added pharmaceutical and biotechnology industries. For example, between 1982 and 2006, one-third of all drugs and nearly 60 percent of promising new molecular entities approved by the FDA cited either an NIH-funded publication or an NIH patent.37

• One study estimated that taking into account the multiplier effect of jobs created in other sectors by NIH-supported research, biopharmaceuticals supported total employment of 3.2 million jobs in 2006, including 686,442 direct jobs and significant source of employment in the U.S. economy.38

• NIH-funded research has contributed to overall gains in average U.S. life expectancy from 1970 to 2000 that were worth an estimated $95 trillion.39

IMAGINE THE FUTURE

If our nation is bold enough to exploit today’s unprecedented opportunities in biomedical research, we will be amazed at what tomorrow brings.

In the world I envision just a few decades from now, the one-size-fits-all approach to medicine will be a thing of the past, and we will use genetic information and environmental exposure data to personalize health care strategies. Doctors will use a patient’s genetic profile – not just weight or age – to determine the best drug and the optimal dose. Even prevention strategies, such as exercise or diet, will be tailored to each person’s unique genetic makeup and environmental circumstances.


We will use stem cells to repair spinal cord injuries, bioengineered tissues to replace worn-out joints, genetic information to tailor therapies with individualized prescriptions, and nanotechnology to deliver these prescriptions with exquisite precision. We will be able to address in unprecedented ways maladies such as diabetes, cancer, and cardiovascular disease, which have affected friends or family of all of us in some way. Contemplate these possibilities:

- An artificial pancreas – perhaps an implantable device – will automatically sense a person’s blood sugar and adjust insulin dosage precisely, and stem cell research may lead to the ability to replace altogether failing insulin-producing cells.
- Oncologists will select cancer drugs based on the precise DNA changes in each person’s tumor, targeting cancer cells precisely, with limited toxicity to healthy cells.
- Personal gene chips will predict risk for high blood pressure and heart disease, and doctors will routinely use minimally invasive image-guided procedures to preempt heart disease.

I also dream of a day when, in ways yet to be discovered, we will be able to prevent Alzheimer’s, Parkinson’s, and other diseases that rob us much too soon of family and friends.

Just imagine what such a future would mean for our nation and all humankind. This is what keeps NIH in the research marathon, and why we ask you to go the distance with us.

Thank you Mr. Chairman. That concludes my formal remarks.