As Director of the National Institutes of Health (NIH), I am pleased to present the Congressional Justification of the NIH fiscal year (FY) 2014 budget request. This budget request for $31.331 billion total program level reflects the President's and the Secretary's commitment to improving the health of the Nation and to maintaining the Nation's leadership in the life sciences. The request highlights investments in innovative research that will advance fundamental knowledge and speed the development of new therapies, diagnostics, and preventive measures to improve public health. The request will enable NIH to enhance efforts to recruit and retain diverse scientific talent and creativity.

NIH has been advancing our understanding of health and disease for over a century, and its contributions are immeasurable. NIH advances are behind most of the gains this country has enjoyed in public health. Today, scientific and technological breakthroughs generated by NIH research are enabling even more rapid progress to be made in turning discovery into health. For example, HIV/AIDS treatment and prevention strategies produced through NIH research may enable us to realize the first AIDS-free generation in over 30 years. In the not-too-distant future, we can anticipate cancer treatment as precisely targeted to each patient's unique tumor biology. We can envision a future in which advanced prevention strategies allow everyone to have a much better chance of living a long and healthy life.

Investment in NIH is not only an investment in a healthier future for all Americans, it is also an investment in our Nation's economy. NIH plays a critical role in underpinning the Nation's competitiveness in the life sciences. Since the late 1940s, the U.S. has led the world in public support for biomedical research, resulting in a life sciences sector that ranks among the strongest performers in the U.S. economy and assures the Nation's place as a leader in science and technology. At a time when many countries throughout the world are dramatically increasing their investment in science and technology, our Nation continues to invest in biomedical research.

The FY 2014 budget request, a 1.5% increase over FY 2012, will enhance NIH's ability to support cutting-edge research and training of the scientific workforce. The budget request allocates resources to areas of the most extraordinary promise for biomedical research, while maintaining the flexibility to pursue unplanned scientific opportunities and address unplanned health needs.

Support of NIH will allow scientists to continue tackling the most common diseases and disorders—such as cancer, heart disease, HIV, and obesity—and also enable researchers to improve treatments and preventions for those suffering from rare and neglected diseases. In addition, new technologies will accelerate discovery and pave the way for NIH medical innovations to reach more people in the Nation and across the globe. More than ever, NIH has

the opportunity to increase the Nation's capability to prevent disease and improve health for all, while solidifying the Nation's preeminence in the life sciences.

I welcome the opportunity to discuss this budget request and NIH's plans for FY 2014 and the years ahead.

Francis S. Collins, M.D., Ph.D.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Volume 1 – Overview

FY 2014 Budget

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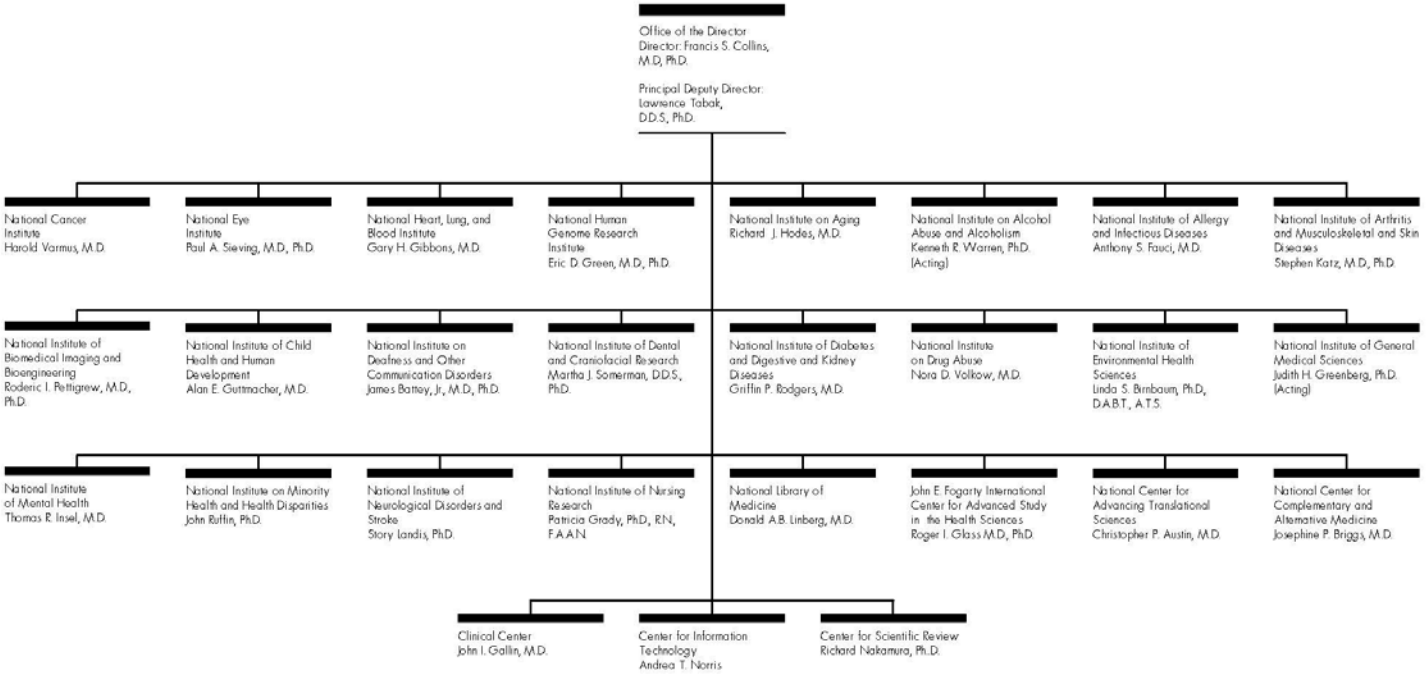
Department of Health and Human Services

National Institutes of Health

Executive Summary

National Institutes of Health



National Institutes of Health

FY 2014 Budget Request

Introduction and Mission

The mission of the National Institutes of Health (NIH) is to advance fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy lives and to reduce the burdens of illness and disability. In pursuit of this mission, NIH conducts or supports research designed to understand the basic biology of human health and disease; apply this understanding towards designing new approaches for preventing, diagnosing, and treating disease and disability; and ensure that these new approaches are available to all.

As the Nation's medical research agency and the largest source of funding for biomedical and behavioral research in the world, NIH plays a unique role in turning basic scientific discovery into tangibles that improve health. NIH's significant and enduring investment in basic research today assures breakthroughs in the health care of tomorrow. To realize such breakthroughs, NIH also invests in research that will translate these basic findings into the delivery of effective health care. This robust research enterprise depends upon NIH's continued innovation as it seeks to recruit and retain the Nation's brightest minds into successful scientific careers. With continued support, NIH will contribute significantly to the economic engine that drives American competitiveness in science and technology, and will make possible the emergence of a Nation in which all Americans enjoy long, healthy lives.

National Institutes of Health
FY 2014 Congressional Justification

All Purpose Table
(Dollars in Thousands)

	FY 2012 Actual [1]	FY 2013 CR	FY 2014 President's Budget	Change from FY 2012 Actual
Labor/HHS Discretionary Budget Authority	**$30,623,259**	**$30,819,454**	**$31,093,776**	**$470,517**
Interior Budget Authority	78,928	79,411	79,411	483
Total Discretionary Budget Authority	**$30,702,187**	**$30,898,865**	**$31,173,187**	**$471,000**
Mandatory Type 1 Diabetes Research	150,000	150,000	150,000	0
Total Budget Authority	$30,852,187	$31,048,865	$31,323,187	$471,000
NIH Program Level [2]	**$30,860,387**	**$31,057,115**	**$31,331,387**	**$471,000**
Number of Competing RPGs	*8,986*	*9,600*	*10,269*	*+1,283*
Total Number of RPGs	*36,259*	*36,343*	*36,610*	*+351*
FTEs	*18,493*	*18,493*	*18,493*	*0*

Note : FY 2012 and FY 2013 figures are shown on a comparable basis to FY 2014.

[1] Includes the Secretary's Transfer of $8.7 million for AIDS authorized by PL 112-74, Section 206 and the Secretary's Transfer of $18.3 million for Alzheimer's disease within NIH.

[2] Includes NLM Program Evaluation of $8.2 million in FY 2012, $8.25 million in FY 2013, and $8.2 million in FY 2014.

OVERVIEW OF BUDGET REQUEST

Total Budget Request
(Dollars in Millions)

	FY 2012 Actual [1]	FY 2014 President's Budget
Total Program Level [2]	$30,860	$31,331
Change from FY 2012 Actual: Dollars	--	$471
Change from FY 2012 Actual: Percent	--	1.5%

[1] Includes the Secretary's Transfer of $8.7 million for AIDS authorized by PL 112-74, Section 206 and the Secretary's Transfer of $18.3 million for Alzheimer's disease within NIH.

[2] Includes Labor/HHS Budget Authority, Interior Superfund Appropriation, Type 1 Diabetes mandatory funds, and NLM Program Evaluation.

The National Institutes of Health (NIH) requests a total program level of $31.331 billion for fiscal year (FY) 2014, $471 million above the FY 2012 level. This funding will allow NIH to continue its pursuit of new knowledge about the nature and behavior of living systems that will improve health. Investment in NIH allows it to create an evidence base to transform health care, from introducing innovative approaches to preventing disease and disability, to increasing the arsenal of tools and techniques used to identify diseases and their risk factors and effectively treat them. Investment in NIH also helps drive the biotechnology sector and maintain the Nation's place as a leader in science and technology. Investment in NIH is an investment in a future in which the Nation leads the world in scientific and technological advancements and all Americans have the chance to lead long, healthy lives.

From a one-room Laboratory of Hygiene in 1887, NIH became the largest funder of biomedical research in the world today. A diverse research enterprise with 27 different Institutes and Centers, NIH research has brought about extraordinary gains in health and quality of life. For example, the last half-century has seen a decline in U.S. death rates from heart disease and stroke by more than 60 percent. Today over 90 percent of children diagnosed with the most common childhood leukemia will survive the disease. Because of NIH research, we have vaccines to protect us from cervical cancer, flu, shingles, and meningitis. And because of gains in treatment and prevention strategies, for the first time in over 40 years, we can begin to realize an AIDS-free generation.

To continue to advance by building on these and many more notable achievements, in FY 2014 NIH plans to capitalize further on the unprecedented opportunities offered by technological advancements that are rapidly accelerating our science. In FY 2014, NIH will focus on generating further basic science findings of today to make possible tomorrow's breakthroughs in health. Simultaneously, NIH will continue its investment in translating basic discoveries into the delivery of more effective health care through a continuum of research with multiple points of translation along the way. This entire endeavor depends upon a robust and exceptional scientific workforce now and in the future. In FY 2014, NIH will further enhance efforts to recruit and retain diverse scientific talent and creativity.

Research not only saves lives, but also results in tremendous cost savings. By reducing disease and disability and by extending healthy lives, NIH research supports greater economic growth by enhancing productivity and economic engagement.[1,2,3,4,5,6,7] In addition, the biomedical research enterprise supported by NIH provides a foundation for the Nation's competitiveness in the life sciences. Many countries throughout the world are increasing their investment in science and technology. Investing in NIH contributes significantly to the competitive strength of the U.S health industry and the science and technology sector in an increasingly global market.

Theme 1: Today's Basic Science for Tomorrow's Breakthroughs

Role of the public domain in basic research and NIH's specific contribution

Investments in basic biomedical and behavioral research make it possible to understand the causes of disease onset and progression, identify associated risk factors, design preventive interventions, develop better diagnostic tests, and discover new cures and treatments. From the incremental advances in our understanding of a given disease, to the groundbreaking discoveries that revolutionize our approaches for treating or preventing it, investments in basic research have produced and will continue to produce profound and long-lasting rewards and benefits to public health. Therefore, support of a broad, basic research portfolio is a critical component of fulfilling the NIH mission.

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[1] *Toole, A. "Does Public Scientific Research Complement Private Investment in Research and Development in the Pharmaceutical Industry?" J. Law. Econ.* ***50****, 81–104 (2007).* http://sciencepolicy.colorado.edu/students/envs_5100/Toole2007.pdf

[2] *Battelle Technology Partnership Practice "Economic Impact of the Human Genome Project" 2011.* http://battelle.org/docs/default-document-library/economic_impact_of_the_human_genome_project.pdf?sfvrsn=2

[3] *Chatterjee, A. and DeVol, R. C. "Estimating Long-Term Economic Returns of NIH Funding on Output in the Biosciences" Milken Institute, 2012.* http://www.milkeninstitute.org/publications/publications.taf?function=detail&ID=38801361&cat=

[4] *Toole, A. "The Impact of Public Basic Research on Industrial Innovation: Evidence from the Pharmaceutical Industry" Res. Policy,* ***41****, 1–12 (2012).* http://dx.doi.org/10.1016/j.respol.2011.06.004

[5] *Blume-Kohout, M. E. "Does Targeted, Disease-Specific Public Research Funding Influence Pharmaceutical Innovation?" J. Policy Anal. Manage.* ***31****, 641–660.* http://onlinelibrary.wiley.com/doi/10.1002/pam.21640/pdf

[6] *Demaerschalk, B. M. and Yipp, T. R. "Economic Benefit of Increasing Utilization of Intravenous Tissue Plasminogen Activator for Acute Ischemic Stroke in the United States" Stroke* ***36****, 2500–2503 (2005).* stroke.ahajournals.org/cgi/pmidlookup?view=long&pmid=16224087

[7] *Johnston, S. C. "The Economic Case for New Stroke Thrombolytics" Stroke* ***41****, S59–S62 (2010).* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2955402/

In response to its mandate, NIH will take on critical scientific challenges whose solutions will continue to drive the engine of discovery and innovation. Often these challenges are ones that NIH is uniquely poised to pursue because other sources are unwilling or unable to undertake them. The following are several examples of such challenges in basic research.

Unlocking the Mysteries of the Brain

Neurological and psychiatric disorders such as Alzheimer's disease, Parkinson's disease, autism, schizophrenia, and traumatic brain injury exact a tremendous toll on society, yet their underlying pathologies remain unknown due to the great complexity of the human brain. This complexity was once thought to be beyond the reach of scientific understanding; today, however, tremendous strides in neuroscience have brought forward remarkable new opportunities for unlocking these mysteries. In partnership with other government agencies, academic institutions, and the private sector, NIH is poised to capitalize on these advances to revolutionize our understanding of the brain's structure and function.

The Human Connectome Project: Within the last decade, several non-invasive imaging techniques have emerged that enable researchers to study how the brain is structurally and functionally organized. The NIH Human Connectome Project, spearheaded by the NIH Blueprint for Neuroscience Research team, harnesses these new technologies to provide the first ever systematic map of the connections within the human brain. Information from these studies will be freely shared with the scientific community in a user-friendly database. The first phase of this effort was completed in 2012 and involved 36 investigators across 11 institutions working collaboratively to optimize data acquisition and analysis methods. The next phase of the project involves collecting data from a cohort of 1,200 twins and non-twin siblings using a variety of novel imaging technologies, along with blood samples in an effort to relate brain connectivity with genetic information. The Connectome project is expected to help answer fundamental questions about how genes influence brain connectivity, and how this in turn relates to mood, personality, and behavior. Individual variability in brain connections underlies the diversity of our thinking, perception, and motor skills, so understanding these networks promises advances in brain health.

Optogenetics: Much brain circuit activity happens so quickly and at such a minute scale that it can elude detection. To unravel the intricate workings of brain circuits with extreme precision, NIH-supported neuroscientists have developed a novel method to reversibly activate and inactivate neurons in experimental models. By combining advanced genetic and optical techniques, scientists can insert light-sensing proteins into neurons and then use pulses of light to turn on or off specific neuronal pathways. Using this method, NIH researchers can precisely control biological events in targeted cells of living tissue. For example, NIH-funded researchers using optogenetics in the mouse brain have identified a distinct brain circuit that seems to switch anxiety off and on. These new tools can be used with existing imaging approaches in living animals to gain insights into how the organization of the brain underlies complex functionality such as mood and thought.

Brain Research through Application of Innovative Neurotechnologies: While technological innovations have greatly contributed to our expanding knowledge of brain structure and function, understanding the human brain will require tools that allow researchers to actively record signals from brain cells at the speed of thought. This cannot be achieved with the tools that are currently available to neuroscientists, but the intersection of evolving fields such as nanoscience, imaging, engineering, informatics, etc., hold great promise for increasing these capabilities. In FY 2014, NIH will begin its support of the Brain Research through Application of Innovative Neurotechnologies (BRAIN) Initiative, in order to develop a deeper understanding of brain function through the creation of new tools capable of examining the activity of the millions of nerve cells, networks, and pathways in the brain in real time. By measuring activity at the scale of circuits and networks in living organisms, we can begin to translate data into models that will decode sensory experience, motor planning, and, potentially, even memory, emotion, and thought. NIH is embracing a collaborative approach in tackling this challenge, working with researchers from across the country, industry, foundations, and other government agencies including the Defense Advanced Research Projects Agency and the National Science Foundation. Successful completion of the BRAIN Initiative could revolutionize the field of neuroscience and set the stage for major advances in diseases such as Alzheimer's, Parkinson's, autism, schizophrenia, depression, and epilepsy.

Single Cell Biology

Classically, biological experiments have been performed on groups of cells, under the assumption that all cells of a particular type are identical and perform identical functions. For example, kidney cells make up filtering units called nephrons, and the assumption has been that all of these are structured identically and perform the same function. However, powerful new research methods of studying single cells have now shown this assumption to be incorrect. Individual cells within the same population, such as those of cancerous tumors, may differ dramatically from one another, and these differences can have important consequences for the health and function of the entire population of cells. The human brain is a key example of an organ where individual cells take on specialized functions (see description of the BRAIN Initiative above). Because of this variability between cells, it is not possible to gain a full understanding of how the brain works based on studying blocks of tissue representing millions or billions of cells. As part of an effort to foster new approaches to discovering the fundamental underpinnings of health and disease, NIH has increasingly focused on understanding cellular function at the level of the individual cell.

NIH supports a wide array of projects that can systematically describe the structure and function of a cell, define normal cell-to-cell variation, measure the impact of environmental perturbations, understand cellular responses in the larger context of tissues and networks, and overcome limitations in measurement approaches. As just one example, scientists have discovered that cells of the immune system with similar surface markers can express different sets of genes, which makes the cells respond differently to vaccines. The NIH Common Fund's new Single Cell Analysis program seeks to overcome current impediments in understanding single cell biology by focusing on opportunities in the evaluation of cellular heterogeneity, exceptionally innovative tools and technologies for single cell analysis, and accelerating the integration and translation of technologies to characterize biological processes.

By examining the specific structural and functional properties of individual cells, scientists are revealing new insights into how tissues and organs function. NIH will continue its mission to foster cutting edge research of single cell biology by identifying the challenges that the research community faces and providing the investigators with incentives and tools to overcome the challenges. Discoveries resulting from single cell biology research will ultimately lead to superior diagnostics and groundbreaking treatments for diseases.

Epigenomics

Epigenomics is the study of DNA modifications as well as modifications of proteins associated with DNA. These modifications do not involve changes in the underlying nucleotide sequence, but rather involve modifying changes to the DNA, such as the addition of methyl groups to nucleotides or other nucleotide or histone modifications. The changes regulate the expression of gene products in response to both environmental factors and extracellular stimuli. Because these modifications, such as DNA methylation and histone modification, result in differences in gene expression, they play a role in development, aging, health, and disease and are therefore prime targets for therapeutic interventions. A deeper understanding of epigenetic processes will enable researchers to make significant strides toward understanding and treating many diseases including cancers, obesity, depression, and addiction, in addition to acquiring a better understanding of the role of the environment in regulating genes associated with health and disease.

Winning the Battle Against Alzheimer's Disease

As many as 5.4 million Americans suffer from Alzheimer's disease (AD), a progressive brain disease that slowly destroys cognitive functions including memory and the ability to reason and think. At the same time, millions of American families struggle with the physical, emotional, and financial costs of caring for a loved one with AD. NIH, with the National Institute on Aging (NIA) taking the lead, supports a number of studies aimed at enabling us to better understand, diagnose, prevent, and treat AD. The latest advances in AD research include:

- Recent NIH-supported research suggests that AD pathophysiology could involve a progressive spreading of pathology from neuron to neuron in selectively vulnerable regions of the brain. Investigators found that misfolded tau protein—a pathological hallmark of the disease—spreads across subsets of neurons by way of the synapses that the neurons had formed with each other.
- A recent NIH-funded proof-of-concept study used cell reprogramming techniques to create neurons from the fibroblasts—a type of skin cell—of healthy individuals and patients with late onset AD as well as familial AD. Compared to neurons derived from healthy individuals, human induced pluripotent stem (iPS) cell-derived neurons from patients with late onset or familial AD had higher levels of amyloid-β and other indicators of AD, providing a novel platform for drug screening.
- Common variants of the ApoE gene are strongly associated with the risk of developing late-onset AD (the more common form of the disease), but the gene's role in the disease has been unclear. Now, NIH-funded researchers have found that in mice, having the most risky variant (e4) of ApoE damages the blood vessels that feed the brain.
- Researchers found that bexarotene, an FDA approved drug for a form of skin cancer, rapidly but transiently reduces the amount of β-amyloid, possibly through interaction with ApoE, within the brain and reverses cognitive and behavioral abnormalities in mice. This finding provides new insight into mechanisms underlying AD pathology and identifies new candidate targets for intervention. Human trials of bexarotene have just begun.
- In a recent, highly promising pilot trial, a nasal-spray form of insulin delayed memory loss and preserved cognition in people with cognitive deficits ranging from mild cognitive impairment to moderate AD. A larger-scale study to confirm and extend these results is getting underway.
- NIH is partnering with private industry and a non-profit research institute to launch a 5-year clinical trial for a promising AD treatment. The trial will test whether a monoclonal antibody named crenezumab can halt or slow the progression of Alzheimer's in cognitively healthy people who are nearly certain to develop the disease because they carry a known genetic mutation. This represents the first time a drug will be tested before the onset of Alzheimer's systems and, if successful, would shape future drug development in the AD field.

In May 2012, HHS released a national plan to fight AD, which was called for in the National Alzheimer's Project Act. NIH's implementation of the plan will be informed by recommendations from the Alzheimer's disease Summit held in May 2012. To advance the progress of research, NIH will enable rapid sharing of data, disease models, and biological specimens, and it will promote the building of new multidisciplinary translational teams and create virtual and real spaces where these teams can operate. NIH will also establish new public-private partnerships to speed drug development by repurposing abandoned compounds.

Recent research findings indicate that epigenetics may also account for some inherited traits and diseases, which would mean that the DNA sequence itself is not the only carrier of heritable information. Epigenetic heritability may help explain issues in human disease that are currently unclear, such as the presence of a disease in only one identical twin, the differences in disease susceptibility between males (e.g., to fragile X syndrome) and females (e.g., to lupus), and significant fluctuations in the course of a disease (e.g., bipolar disorder, inflammatory bowel disease, multiple sclerosis). For example, NIH-funded researchers recently found an early epigenetic effect in Alzheimer's disease (AD). They found that a protein called histone deacetylase 2 (HDAC2) accumulates in the brain early in the course of AD both in people with the disease and in mouse models. In mice, the increase in HDAC2 appears to block the expression of genes involved in learning and memory. By reducing the levels of HDAC2, and thereby mitigating the blocking effect, researchers were able to prevent impairment of learning and memory in these mice, suggesting a possible new approach to the treatment of AD in humans.

Since epigenomics represents a critical next phase in understanding the genetic regulation of health and disease, NIH is funding studies of the epigenome in a range of diseases and conditions, including cancer, cardiovascular disease, autism, glaucoma, asthma, aging, and abnormal growth and development. The NIH Common Fund Epigenomics Program consists of a series of complementary initiatives aimed at generating new research tools, technologies, datasets, and infrastructure. One of the initiatives seeks to develop a series of reference epigenome maps, analogous to genome maps, which will be publicly available to facilitate research in human health and disease. It is also designed to evaluate epigenetic mechanisms in aging, development, environmental exposure including physical and chemical exposures, behavioral and social environments, and responses to stress. Additional components aim to develop new technologies for epigenetic analysis of single cells and imaging of epigenetic activity in living organisms. The initiative will also engage the international community in defining standard practices and platforms and develop new laboratory tools.

Opportunities and Challenges Associated with Big Data

With advancing technological and computational capabilities, biomedical researchers are generating a vast amount of data at an unprecedented pace. These large and complex datasets—referred to as Big Data—are generated from an array of devices such as genomic sequencing machines, high-resolution medical imagers, electronic health records, and smart phone applications that monitor patient health. The size of these datasets goes well beyond the familiar mega- and gigabyte domains to the exotic realms of terabytes, petabytes, and yottabytes of information. A terabyte of data would fill about 80,000 file cabinets; a yottabyte would need a trillion more.

The ability to visualize, manipulate, and mine Big Data provides opportunities to enhance our understanding of disease onset and progression, identify new therapeutic avenues, and speed the translation of new discoveries into improved health and health care. NIH supports several initiatives to accelerate the pace of discovery through the use of Big Data. For example, the Human Connectome Project and the BRAIN Initiative (described earlier in this section) are efforts to map neural pathways that underlie human brain function. These will set the stage to

discover abnormal brain circuits that contribute to neurological and psychiatric disorders. The Cancer Genome Atlas project applies large-scale genome sequencing to accelerate our understanding of the molecular basis of cancer. PhysioNet offers free web access to large collections of complex physiologic signals, such as cardiac rhythms and gait dynamics, and related open-source data analysis software to catalyze research advances in the underlying mechanisms of health, disease, and aging.

Sharing Big Data readily and responsibly is a critical step in translating new discoveries into clinical applications. However, real challenges arise when scientists try to visualize, manipulate, or mine complex datasets. The computational foundation required for maintaining, securing, and processing large-scale datasets typically goes far beyond the capabilities of individual investigators. Additionally, a well-trained workforce is essential to realize the full value of Big Data. Education and training efforts are needed to address current and future demands for specialists such as data scientists, computer engineers, and bioinformaticians who have the requisite skills to manage, analyze, store, and preserve complex scientific data. A 2011 analysis by the McKinsey Global Institute for the U.S. Bureau of Labor Statistics found that the U.S. faces a shortage of 1.5 million managers and analysts, including those in biomedical fields, with the skills to understand and make decisions based on the analysis of Big Data.[8]

To address these challenges, NIH is developing the Big Data to Knowledge (BD2K) program, which it plans to launch in FY14. BD2K will support four programmatic efforts: (1) facilitate the broad use and sharing of large, complex biomedical data sets through the development of policies, resources and standards; (2) develop and disseminate new analytical methods and software; (3) enhance training of data scientists, computer engineers, and bioinformaticians; and (4) establish Centers of Excellence to develop generalizable approaches that address important problems in biomedical analytics, computational biology, and medical informatics. In FY14, NIH will invest at least $40 million in the BD2K program through the Common Fund, and each Big Data Center of Excellence will be funded at $2 million to $5 million per year for 3-5 years. As Big Data challenges in biomedical research are shared with other areas of scientific research such as energy and space research, BD2K will also require effective collaboration and coordination with other government agencies tackling similar challenges, including the National Science Foundation and the Department of Energy, as well as privately funded efforts.

Big Data can accelerate the translation of data bytes to bedside applications that advance the detection, diagnosis, and treatment of disease. With proper investments and coordination with other government agencies and private sector stakeholders, the infrastructure and workforce challenges can be overcome to realize the full potential of the data revolution.

Theme 2: Translational Science

NIH supported basic research provides the fundamental body of knowledge for clinical discovery. Translational research uses the knowledge gained from basic discoveries to target newly identified mechanisms for intervention; conduct clinical trials testing the efficacy and

[8] *For more information, see http://www.mckinsey.com/Features/Big_Data.*

effectiveness of these interventions; and seek the means by which interventions are disseminated and implemented broadly and appropriately in the health care system.

NIH supports translational research by providing not only financial and grant support to investigators, but also by creating research resources that can be used by scientists, clinicians, and the public to better enable advances. Access to NIH infrastructure and resources in the form of scientific tools, reagents, services, and information helps researchers turn preclinical research into effective healthcare. Most NIH Institutes and Centers support their own translational support resources, tools, and programs, typically using a disease centered approach. In addition, through the new National Center for Advancing Translational Sciences (NCATS), NIH is helping to catalyze innovations in translational and clinical research using a trans-disciplinary approach, with the goal of enabling both the public and private sector to develop drugs and diagnostics more efficiently.

Regenerative Medicine

Regenerative medicine brings together the life, physical, and engineering sciences to develop functional cell, tissue, and organ substitutes to repair, replace, or enhance biological function that has been lost due to congenital abnormalities, injury, or disease. Reflecting the potential applicability of this approach to a wide range of diseases and disorders, many of the NIH Institutes and Centers support it. In fact, together they provided nearly $1 billion in funds for regenerative medicine in FY 2011. With an aging population come increases in chronic conditions, which could be aided by regenerative medicine approaches. Multi-disciplinary efforts are being employed to address the complexities of repairing or replacing damaged organs and tissues.

Current research efforts include the development of novel biomaterials or scaffolds, the identification of sources of cells and the optimization of their differentiation into desired cell types, the functional assessment of engineered tissues (including new imaging tools for real time assessment), and the design of informatics systems for the design and characterization of engineered tissues. For example, NIH-funded research clinicians have reported success using bioengineered urethras for boys who needed urethral reconstruction. This method uses the patient's own cells combined with a biodegradable scaffold. NIH-funded researchers have also developed a humanized mouse model duplicating human liver function, which will be invaluable in assessing new drugs for toxicity.

One particularly exciting area of regenerative medicine research is work with induced pluripotent stem (iPS) cells; adult skin or blood cells that have been reprogrammed to be able to become nearly any type of cell in the body. NIH supports an exciting array of research projects that use iPS cell technology to help understand disease, spur drug discovery, and pave the way for new cell-based therapies.

The NIH Center for Regenerative Medicine (NIH CRM), which has a central goal of advancing basic and translational research involving iPS cells, is working on a number of initiatives. For example, through a collaboration with a foundation and several cord blood banks, the Center is developing iPS cells from cord blood samples. The iPS cells will be programmed to become

specific types of cells needed to treat blood-related diseases. Researchers will also investigate whether iPS cells can be used to develop blood products that could help meet the demand for blood transfusions during medical emergencies and surgeries. The Center is also working with the Therapeutics for Rare and Neglected Diseases program to develop human neuronal cells to screen a library of compounds from FDA-approved drugs to identify new drug candidates to treat Niemann-Pick Type C, a progressive neurological disease. A major goal of CRM is to develop protocols to test the therapeutic use of iPS cells for various human diseases. Many other collaborations are underway with state-funded stem cell research projects and with research organizations in Japan, India, and Korea.

Another major effort with iPS cells is through the National Institute of Neurological Disorders and Stroke (NINDS), which has supported three multi-institutional consortia focused on generating fibroblast and iPS cells from patients with Huntington's disease, familial forms of Parkinson's disease, and Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's disease). Cell lines developed by these consortia are available through the NINDS Human Genetics Repository at the Coriell Institute. More than 460 fibroblasts and iPS cell lines have been distributed worldwide to academic and industry researchers to support basic and translational science efforts focused on therapeutic advancements for adult-onset neurodegenerative diseases. To further these goals, NINDS has developed funding partnerships with industry, several foundations, and the California Institute for Regenerative Medicine to advance a new research funding announcement focused on the development of tools that will support improvements in iPS cell technologies and disease-modeling.

Research alone is not enough to move a new technology from the lab to the clinic; there are significant regulatory issues that also must be addressed. To help iPS cell technology reach patients as swiftly as possible, the NIH and the Food and Drug Administration (FDA) are working together to help researchers from the public and private sectors gain a better understanding of the regulatory requirements and plan accordingly. For example, NIH and FDA are holding a series of workshops to provide guidance on how to design iPS experiments and present data in ways most conducive to efficient regulatory approval.

Work also continues with other types of cells, including adult stem cells and mature cell types. For example, the National Heart Lung and Blood Institute's Blood and Marrow Transplant Clinical Trials Network was renewed in 2011, so clinical research to improve regenerative hematopoietic stem cell transplants will continue to be supported. Direct reprogramming of mature cells from one lineage to another has emerged as another strategy for generating cell types of interest. NIH-funded researchers recently reprogrammed human fibroblasts into functional neurons, with implications for cell-replacement strategies in neurodegenerative diseases, disease modeling, and neural developmental studies.

Altogether, regenerative medicine is a varied and rapidly developing field; with potential clinical applications emerging quickly from novel technologies.

Developing Better Ways of Crossing the Blood-Brain Barrier

The development of therapeutics for the central nervous system (CNS) has challenged scientists and clinicians due to the difficulty in delivering molecules and genes across the blood brain barrier (BBB) and its extension into the spinal cord, the blood-spinal cord barrier. These barriers protect the CNS by and preventing the entry of pathogens and toxic chemicals from the bloodstream. Modalities for drug delivery through the brain vasculature generally entail the "disruption" of the BBB, either by osmotic means or the use of vasoactive substances. Recent advancements in nanomedicine have led to new strategies based on the use of: (1) lipophilic materials at the nanoscale level (*nanocarriers*) to encapsulate drugs, and (2) drug-delivering *nanoparticles* carrying selective surface ligands that favor the passage into the CNS by targeting the nutrient transport systems present on the BBB (*Molecular Trojan Horses*). The therapeutic potential of these new nanotechnologies has just begun to be explored. Globular tree-like nano-polymers (*dendrimers*) carrying the anti-inflammatory drug N-acetylcysteine have been successfully used in an animal model of cerebral palsy to reduce neuro-injury and improve motor function. Recently, NIH-funded investigators developed a new method for CNS drug delivery that employs an ultrasound beam that when aimed at a brain tumor "excites" dissolvable gas bubbles (*microbubbles*) injected into the bloodstream along with biodegradable nanoparticles bonded to chemotherapy drugs. As the "excited" microbubbles pass through the blood vessels near the tumor site, they vibrate and open pores in the BBB, allowing the drug-bearing nanoparticles to cross into the brain and deliver the drugs near the tumor. Another promising approach is the topical application of drugs attached to *nanowires*, which have shown therapeutic value in the treatment of spinal cord and traumatic brain injury, as evidenced by the increased drug efficacy and penetration, and the significant reduction of BBB breakdown, edema, and other brain complications.

Despite the success of these nanotechnologies, the search for optimal CNS drug delivery strategies remains an ongoing challenge. Important future goals include the development of BBB-permeable radiopharmaceuticals to improve current brain imaging techniques and new approaches for gene delivery to brain tumors that take into account the unique character of brain vasculature.

The National Center for Advancing Translational Sciences

Created in FY 2012, the National Center for Advancing Translational Sciences (NCATS) catalyzes the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. In addition to traditional funding mechanisms, NCATS is also empowered to use the Cures Acceleration Network (CAN) to provide flexible spending authority that allows projects to be managed actively and aggressively via mechanisms similar to those used by DARPA at the U.S. Department of Defense.

Several new NCATS efforts are the result of innovative partnerships with the public and private sectors. NIH is partnering with the FDA and DARPA to develop 3-D tissue chips, which mimic human tissues and organs, to evaluate the efficacy and safety of drug candidates. NIH is

collaborating with the FDA and the Environmental Protection Agency to profile environmental chemicals and approved drugs for potential toxicity through the Tox21 Initiative.

NIH is also pursuing collaborative partnerships with the private sector to address challenges in the therapeutic development process. In May 2012, NCATS announced a new collaborative program between the biomedical research community and pharmaceutical company partners to explore new uses for discontinued proprietary drug candidates across a broad range of human diseases. Under the Discovering New Therapeutic uses for Existing Molecules Program, NCATS will allocate up to $20 million a year to support pre-clinical and proof-of-concept clinical studies to test drug candidates for use against new disease targets. The response has been gratifying – applications have been submitted to seek new uses for every one of the 58 compounds made available for repurposing.

NCATS also supports research aimed at accelerating new treatments for rare and neglected diseases. The Therapeutics for Rare and Neglected Diseases (TRND) program supports research collaborations by providing scientific investigators access to specialized expertise and resources to conduct milestone driven drug development research to the point where projects can be handed off to biotechnology or pharmaceutical companies. As an example, NIH, through the National Heart, Lung, and Blood Institute (NHLBI) and NCATS/TRND, is currently partnering with the biopharmaceutical company AesRx to conduct clinical trials at the NIH Clinical Center using Aes-103, a promising compound to treat Sickle Cell Disease (SCD), a neglected disease. The single current FDA approved drug, hydroxyurea, has significant side effects and cannot be administered to children.

NCATS supports and coordinates rare disease research through the Office of Rare Diseases Research (ORDR). In collaboration with several NIH institutes and centers, ORDR also manages the Rare Diseases Clinical Research Network, which supports training, pilot projects, and clinical research, and the Genetic and Rare Diseases Information Center, which provides access to comprehensive information on rare and neglected diseases.

Precision Medicine to Combat Cancer

Despite the many advances made in cancer prevention, diagnosis, and treatment, it remains the second most common cause of death in the U.S., accounting for one in four deaths and exceeded only by heart disease. While overall U.S. death rates from all cancers for men and women declined from 2003-2007, cancer remains an enormously complex set of diseases, with prevention, detection, and treatment approaches yielding variable benefit for different cancer types and persistent unexplained cancer-related health disparities. For many years, standard cancer treatment relied on radiation and chemotherapy agents, which are systemic therapies, attacking both cancerous and normal bystander cells. With advances in genomic medicine, breakthroughs are now appearing in precision medicine, so that therapy can precisely target each patient's unique tumor biology.

NIH continues to be a leader in supporting genomic research that has the potential to revolutionize cancer therapy. As an example, NIH-supported research led to the identification of a mutation that, while only found in five percent of lung cancers, led to the development of crizotinib, a targeted therapy that had dramatic response rates in clinical trials, leading to its rapid approval.

A key initiative to advance precision medicine for cancer is NIH's Cancer Genome Atlas (TCGA), a joint effort of the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI). TCGA is the largest and most comprehensive characterization of all relevant genomic alterations in a variety of human cancers. A publicly accessible database, it promises to open new avenues for developing biomarkers and other targeted therapies. TGCA researchers have already published the results of their analysis of brain tumors, colon, rectal and ovarian cancers, with many more comprehensive analyses in the pipeline.

NIH's continued investment in genomic medicine for cancer will be critical in continuing to open new therapeutic avenues and catalyzing a new approach to cancer therapeutics. NIH support has allowed for an increase in the capacity of genomic sequencing centers, making new data available to researchers all over the world that may lead to a better understanding of disease and the identification of novel therapeutics. The tools provided by such analyses may enable selective use of "traditional" therapies to maximize the likelihood that they will be effective, lead to the development of new targeted therapies, and potentially lead to combination therapies that will provide new avenues of treatment for patients.

Empowering a National Clinical Research Network

Now is an opportune time for a bold strategy to support the conduct of clinical research in the U.S. that builds on remarkable advances underway in the Nation's use of electronic health records (EHRs), in computing and data storage capabilities, and in the realization that greater knowledge can be gained from each and every patient's clinical experience. To capitalize on these developments, a national effort is being launched to establish a nimble, cost-efficient network – the National Clinical Research Network – that will bring together tens of millions of patients who agree to participate in a broad range of clinical research studies, including observational and interventional trials. This bold initiative will require the participation and collaboration of patients, researchers, health care delivery organizations, EHR providers, payers, and government agencies.

In addition to advancing research to improve diagnosis, treatment and management, and prevention, the Network would also work on innovating the conduct of clinical research through the development of novel study methods and trial designs, including the use of personal electronic devices for follow-up; low-cost clinical trials; hybrid approaches that integrate randomized controlled trial and observational study research designs; and common data elements and standardized clinical vocabularies. The following examples illustrate the types of studies that the Network would be particularly well positioned to conduct:

- *Better Management of Multiple Chronic Conditions (MCC).* Health care management of patients with MCC is complex. Limited information is available regarding how interventions for one condition affect outcomes related to another or how safety and effectiveness of treatments for a single disorder can be affected by coexisting conditions and their respective treatments. Given the number of consented, well characterized patients that would be available through the Network, testing of multiple interventions could be carried out for a variety of combinations of chronic conditions. Trials to evaluate the effects of different patient management decision strategies on outcomes in such patients could yield significant scientific advances in the management of multiple chronic conditions.

- *Better Treatment of Chronic Pain.* The Network would enable the tracking of many different outcomes of interest at both the system and patient levels. For example, integrated information systems could track pharmacy data and prescribing practices and patient-reported measures of pain and functional impairment to identify best practices for pain management and preventing the development of dependence.

- *Enhancing Predictive Validity of Health Measures for Minority Groups.* Risk scores for many disorders are largely validated in white populations. With millions of consented subjects from diverse populations, the Network would provide sufficient power to develop validated risk scores for multiple population sub-groups. With improved health measures, preventive care could be more efficiently made available to individuals at highest risk.

Efforts to design this Network are already underway, including potential collaboration with the Patient-Centered Outcomes Research Institute (PCORI) and other government agencies to help develop interoperable networks to support adaptable, reusable, scalable, and sustainable health data. Uniquely poised to contribute to this Network's success, NIH will initiate several pilot efforts 14 to augment and complement Network activities:

- *Creating a Biorepository*. NIH will begin planning for the creation of a repository of clinical samples linked to EHR data to help address some of our Nation's most vexing health questions.
- *Increasing Patient Participation*. NIH will develop models to expand patient awareness of the value of the learning health care system and the knowledge that could be gained by broader participation in research and data analysis.

- *Addressing Big Data.* NIH is supporting efforts in the management of large and complex data sets, including through Centers of Excellence funded to develop a sophisticated interface for the new Network.
- *Increasing Outreach to Underserved Populations.* In addition to the involving large health care delivery organizations in the Network, NIH will explore mechanisms to ensure that health care systems serving rural or underserved populations are also engaged.

New Models for Scientific and Technological Collaboration

NIH is working to re-engineer the translation process through engaging stakeholders from the public and private sectors to aid in identifying and developing new collaborative models that leverage resources and specialized expertise from multiple sectors. An example is the effort underway to establish a precompetitive consortium of scientists in industry, academia, and government to work together to improve target validation, a significant challenge in the therapeutic development process. The large number of potential therapeutic targets emerging from genomics and other basic science discoveries represents an important opportunity for translational science. This wealth of information and related technologies, however, also presents a processing and informatics challenge to target validation. In order to realize the potential of these discoveries, faster, more accurate processes and techniques are needed to identify the most promising targets. NIH is currently working with the biopharmaceutical industry and academia to expand the precompetitive space to include target validation and leverage the knowledge, strengths, and expertise of multiple sectors. Under the guidance of a joint NIH-industry steering committee, working groups are exploring ways to work collaboratively to improve target validation research methods and advance target validation in several disease areas.

Theme 3: Recruiting and Retaining Diverse Scientific Talent and Creativity

Enhancing Diversity in the Biomedical Research Workforce

NIH is strongly committed to maintaining a diverse biomedical research workforce and has supported diversity programs for more than 30 years in order to achieve this goal. While progress has been made in some areas, these programs have not been as broadly successful as NIH would like them to be.

Steps taken to enhance workforce diversity include an initiative to provide greater opportunities for junior faculty from a broader range of institutions to participate in peer review panels, where young researchers can gain insight into the grant review process and improve their chances of successfully competing for an NIH grant. In addition, in June 2012, the NIH Advisory Committee to the Director (ACD) issued a report[9] that outlined recommendations on further actions that the NIH should take to increase the representation of underrepresented groups in the biomedical research workforce. In response, NIH will work to continue creating an environment

[9] *For more information, see http://acd.od.nih.gov/dbr.htm.*

that fosters and promotes recruitment and training of people traditionally underrepresented in the biomedical research workforce through the Biomedical Research Workforce Diversity Initiative.

The main goal of the Diversity Initiative is to increase the diversity of the NIH-funded workforce. The centerpiece of the initiative is the ***Bu****ilding* ***I****nfrastructure* ***L****eading to* ***D****iversity (BUILD) Program* that is designed to provide relatively under-resourced institutions with the opportunity to focus resources on educating its students, many of whom are from disadvantaged backgrounds and backgrounds nationally underrepresented in biomedical research to move into graduate programs for biomedical research. The program will consist of a consortium of approximately 10 institutions across the country that will enroll around 600 students nationwide. The BUILD program will include:

- Rigorous mentoring in research for two summers (during college) and up to two years (post-graduation),

- Tuition scholarships and stipends, for up to two years of undergraduate studies and additional loan repayment once in graduate school,

- Salary offset and other infrastructure support for key faculty responsible for undergraduate research training,

- Resources for highly effective mentors to train new mentors, and

- Support for an "innovation space" to enable organizations to develop novel approaches for increased diversity in PhD programs.

Additionally, the new Diversity Initiative will do the following:

- Create a single, nationwide consortium, the National Research Mentoring Network (NRMN), that will connect students, postdoctoral fellows, and faculty to experienced mentors, develop standards for good mentorship, and provide training to individuals interested in learning how to become better mentors;

- Establish a BUILD and NRMN Coordinating and Evaluation Center to link all of the program participants;

- Establish an ACD Working Group on Diversity, composed of scientists who are themselves diverse and charged with advising the NIH Director and ICs on effective programs that address disparities in research awards;

- Recruit a Chief Officer for Scientific Workforce Diversity, and make changes to the hiring process for tenure-track investigators to include more underrepresented candidates in the pool of candidates;

- Conduct studies related to the review and funding of grants, to understand potential bias, and test various bias and diversity awareness training programs for NIH Staff to determine the most effective approaches; and

- Develop better means of tracking all trainees and enhance data collection capabilities with respect to data on Hispanic sub-populations, individuals with disabilities, socioeconomic status, and education.

Encouraging Innovation

Innovation is fundamental to scientific advancement, and NIH encourages innovation through many cutting-edge programs, including the following:

- The NIH Director's Early Independence Award was established to provide a mechanism for exceptional, early career scientists to omit traditional post-doctoral training, and move into independent research positions at U.S. institutions directly upon completion of their graduate degrees (Ph.D., M.D., or equivalent).

- The NIH Director's New Innovator Award addresses two important goals: stimulating highly innovative research and supporting promising new investigators. Many new investigators have exceptionally innovative research ideas, but do not have the preliminary data required to fare well in the traditional NIH peer review system. As part of NIH's commitment to increasing opportunities for new scientists, the agency has created this award to support new investigators who propose innovative projects that have the potential for unusually high impact.

- The NIH Director's Pioneer Award Program is designed to support individual scientists of exceptional creativity who propose pioneering—and possibly transforming approaches—to major challenges in biomedical and behavioral research. To be considered pioneering, the proposed research must reflect ideas substantially different from those already being pursued in the investigator's laboratory or elsewhere.

- The NIH Director's Transformative Research Award was created specifically to support exceptionally innovative and/or unconventional research projects that have the potential to create or to overturn fundamental paradigms. These projects tend to be inherently risky and may not fare well in conventional NIH review, but could be extremely important if successful.

In addition to these NIH-wide programs, many of the NIH Institutes and Centers have developed their own programs for fostering innovation in science specific to their respective missions. For example, the National Institute of Drug Abuse (NIDA) has created the NIDA Avant-Garde Award Program for HIV/AIDS Research. This program supports individual scientists of exceptional creativity who propose high-impact research that will open new areas of HIV/AIDS research and/or lead to new avenues for prevention and treatment of HIV/AIDS among drug abusers.

Assessing the Overall Biomedical Workforce

In December 2010, Dr. Collins charged the ACD with examining the future of the biomedical research workforce in the U.S. The group was asked to recommend actions NIH should take to ensure a diverse and sustainable biomedical and behavioral research workforce. The findings and conclusions of the study were presented in June 2012.[10] The group concluded that: the combination of the steady production of Ph.D.'s trained in the U.S., inadequate growth in career opportunities in biomedical research, increased influx of foreign-trained Ph.D.s, and the aging of the academic biomedical research workforce make launching a traditional, independent, academic research career increasingly difficult; the long training time and relatively low early-career salaries when compared to other scientific disciplines and professional careers may make the biomedical research career less attractive to the best and brightest of our young people; and, current training programs do little to prepare people for anything besides an academic research career, despite clear evidence that a declining percentage of graduates will find such positions in the future.

NIH is implementing the following measures in response to the ACD study:

- Establishing a grant program to encourage innovative training approaches, providing more information about various career pathways,
- Improving graduate student and postdoctoral training by putting individual development plans in place for all extramural students and postdoctoral fellows; working to reducing the length of graduate training, and providing pre-doctoral fellowships from all ICs so all areas of science are covered.
- Increasing postdoctoral stipends and considering policies on benefits,
- Increasing support for awards that encourage independence including the K99/R00 Pathway to Independence awards and the Early Independence awards,
- Developing a simple and comprehensive tracking system for trainees,
- Revising training grant review processes so that study sections consider a range of career choices and take into account the outcomes of all graduate students and postdoctoral fellows in relevant programs,
- Initiating a discussion with the community to assess the number of NIH trainees and the support of salaries, and
- Creating a functional unit at NIH to continue to assess the biomedical research workforce.

[10] *For more information, see http://acd.od.nih.gov/bwf.htm.*

Pursuing a Global Health Agenda

In a world in which emerging infections can easily cross national boundaries and non-communicable diseases are taking an increasing toll on low- and middle-income countries just as they are in high-income countries, NIH pursues a global health agenda that is truly universal in scope. To address the many risk factors common to all people and to find new and better ways of intervening to prevent and treat, we need a coordinated approach to bring science to bear on health problems throughout the world. NIH has taken a leadership role in addressing this challenge.

Global cooperation to evaluate diagnostic, preventive, or therapeutic procedures enables more rapid recruitment of patients and results in a greater degree of international acceptability of results. For decades, the notion of controlling or ending the HIV/AIDS pandemic has been a distant aspiration. But all that is changing. As described more fully below in *Securing an AIDS-free Generation*, NIH research partnerships in Brazil, Africa, India, and Southeast Asia, have produced scientifically validated treatment and prevention strategies, suggesting that the end of the pandemic is feasible.

Non-communicable diseases now account for 63 percent of deaths worldwide, principally due to heart disease, diabetes, cancer, and chronic respiratory diseases. The World Health Organization predicts that, in the next decade, this number will grow by 17 percent overall and by 24 percent in Africa. NIH programs are beginning to help low-resource countries build capacity to fight the growing burden of chronic diseases. For example, NIH supports collaborative diabetes research projects in India, a country that has the highest number of diabetics in the world. In South Africa, NIH-supported researchers are looking at cost-effective ways to screen for heart disease. Ongoing research in South Asia on the effects of household air pollution may lead to a reduction in chronic respiratory disease. Egyptian and American investigators are working together to find new drug pathways to treat inflammatory breast cancer.

In addition to global health research efforts, NIH is supporting global health research training in the U.S. and abroad; a critical step to ensure that countries can address their own health challenges. Many low- and middle-income countries lack sufficient numbers of trained scientists and researchers. To address this disparity, NIH's Common Fund Program joined with PEPFAR to launch the Medical Education Partnership Initiative (MEPI) to help foreign institutions in Sub-Saharan Africa develop or expand and enhance models of medical education to help build clinical and research capacity. Building in-country research capacity allows for the creation of an international cadre of scientists who can work together to apply scientific innovations to global health problems. One such approach is NIH's support for population-based studies of common, chronic disorders in Africa. The Human Heredity and Health in Africa (H3Africa) Initiative, a collaborative effort with the Wellcome Trust in the UK, aims to facilitate a contemporary research approach to the study of genetic and environmental determinants of common diseases with the goal of improving the health of African populations.

NIH's continued support for global health research and training through initiatives such as MEPI and H3Africa have benefits far beyond the countries in which they occur. In an increasingly connected world, what we learn in Sub-Saharan Africa or in Southeast Asia will apply to the health of populations around the globe.

Theme 4: Restoring American Competitiveness

Economic Benefits of Improving Health

Significant, measurable advances in the diagnosis, treatment, and prevention of human disease provides the primary rationale for publicly funded biomedical research, conducted or sponsored by the NIH and other federal agencies. In brief, new knowledge, techniques, methods, and technologies in biomedicine benefit the lives of the healthy and the sick. However, improvements in health maintenance and preventing, diagnosing, and treating human disease not only yield longer lives and lives less burdened by disease and disability—they also generate quantifiable economic benefits for patients, their families, and society at large.

Research-fueled reductions in death rates from diseases that rank as the nation's leading killers translate into extended, healthier lives. In the past sixty years, death rates from heart disease, the leading cause of the death in the U.S., have been reduced by more than 65 percent. From 1999 to 2009, the death rate for cancer, the second leading cause of death, dropped nearly 12 percent and, in a similar time period, the death rate for stroke fell by 34 percent.[11] Research-fueled progress also extends lives: since 1900, life expectancy in the U.S. has increased dramatically. A child born today can look forward to an average life span of 78.7 years.[12]

The economic value of these gains in average life expectancy has been the focus of analysis and debate. Using an innovative methodology, economists at the University of Chicago, K.M. Murphy and R.H. Topel, estimated the total dollar value of gains in longevity for the U.S. population for the period 1970 to 1998 at $72 trillion dollars.[13] Murphy and Topel have also attempted to capture the value of continued decreases in the death rate attributable to particular causes: for example, according to their analysis, every one percent decrease in the death rate from cancer was estimated to save about $440 billion per year—approximately four percent of the U.S. gross domestic product.

In addition to decreases in disease-specific mortality rates and increases in the life span, biomedical research also yields new, more therapeutically effective—and more cost effective—approaches to diagnosing and treating disease. For example, research shows that treating patients at moderate risk for cardiovascular disease with statins can prevent as many as 27,000 deaths from heart disease every year and reduce annual medical spending by up to $430 million.[14] Influenza costs an estimated $87.1 billion in direct medical costs and lost productivity, and flu vaccines help to combat this economic burden, especially among high-risk populations (children and the elderly). One study showed that in a region with a universal influenza vaccination policy, cases and deaths dropped by 61 percent and 28 percent respectively. Against the backdrop of mounting concern over the intertwined epidemics of

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[11] *Research America: The Impact of Health Research – Research: An Economic Driver that Saves Lives and Money, 2012.*
[12] *CDC, National Vital Statistics Reports—Deaths: Preliminary Data for 2011, October 10, 2012.*
[13] *Murphy, KM and Topel, RH. Measuring the Gains from Medical Research: An Economic Approach. The University of Chicago Press, 2003.*
[14] *Research America: The Impact of Health Research – Research: An Economic Driver that Saves Lives and Money, 2012 Update.*

obesity and type-2 diabetes, NIH-funded research has shown that low-cost lifestyle changes can reduce the risk of diabetes. This is especially welcome news given that patients with the disease incur significant medical costs, twice as high as individuals without diabetes.[15]

Reversing the National Epidemic of Obesity

Approximately one-third of U.S. adults are considered obese based on body mass index (BMI), putting them at increased risk for type 2 diabetes, heart disease, stroke, many forms of cancer, osteoarthritis, and fatty liver disease. Even more worrying, however, is the increase in childhood obesity; nearly 17 percent of children and teens ages 2 through 19 are obese, a prevalence that has more than tripled over the past three decades. Recently reported results of the NIH-funded TODAY study demonstrated how difficult it is to treat type 2 diabetes in children, making it urgent to prevent obesity in youth, so that they do not develop type 2 diabetes and its devastating consequences.

Evidence-based approaches to making—and sustaining—changes in diet, exercise, and the built environment are being developed. For example, researchers funded by NIH have demonstrated that sustained weight loss in adults can be achieved through weight loss coaching either in-person or remotely (via phone, Web, and email contact) and with support from primary care providers. The NIH-supported Look AHEAD study showed that weight loss and increased fitness from a lifestyle intervention slow the decline of mobility in obese adults with type 2 diabetes—findings that have great implications for quality of life and avoiding disability as we age.

Surgical interventions offer another means of addressing obesity. Researchers recently found that bariatric surgery can help control type 2 diabetes more effectively than medical therapy alone in obese individuals, for at least a year. Other ongoing studies are assessing the long-term safety and efficacy of bariatric surgery for weight loss and other conditions.

In the laboratory, NIH-funded researchers are examining the process that causes white fat to mimic energy-burning brown fat and muscle. Exercise induces muscle to produce a newly-discovered hormone, irisin, that drives white fat cells to take on characteristics of calorie-burning brown fat tissue (via gene expression changes). Future research will determine whether irisin could be used therapeutically to achieve health benefits similar to those of exercise.

NIH remains committed to supporting obesity research. Examples of ongoing research challenges include: designing and evaluating interventions not only for behavior change, but also for changing the environment to make the healthy choice the easy, affordable, and appealing choice for adults and children; intervening early to promote healthy lifestyles for very young children and overweight/obese pregnant women; reducing health disparities in obesity (racial/ethnic, socioeconomic, geographic); defining molecular pathways that control weight and appetite to develop more effective interventions; and, understanding how diet, activity, sedentary behavior, sleep, genetics, and potentially other factors interact to increase risk of obesity-associated diseases, including type 2 diabetes, cardiovascular disease,

NIH Role in Supporting the Science and Technology Sector

[15] *Research America: The Impact of Health Research – Research: An Economic Driver that Saves Lives and Money, 2012 Update.*

Since the late 1940s and early 1950s, the U.S. has led every developed country in the world in public support for biomedical research. Built on strong, bipartisan consensus, the U.S. Congress steadily increased support for NIH and biomedical research beginning in the late 1940s. From 1945 to 1961, public support for biomedical research increased 150-fold, reaching a grand total of $460 million; by the late 1960s that support had increased to $1 billion. From 1998 to 2003, funding for the NIH doubled.

NIH funding generates a cascade of benefits throughout the economies of the Nation as a whole, of key regions, and of each of the 50 states and the District of Columbia. Studies, funded by external organizations, of the 2010 and 2011 NIH budgets testify to this fact. In a May 2011 i, United for Medical Research (UMR) calculated that $26.6 billion in NIH extramural funding in 2010 directly and indirectly supported 487,900 jobs nationwide.[16] According to a recent update of the UMR report, NIH remained "a powerhouse driver of economic activity and jobs" in 2011. The $23.7 billion spent by NIH extramurally in the 50 states and the District of Columbia in 2011 directly and indirectly supported 432,094 jobs. Thirteen states showed NIH-supported employment of 10,000 or more and nearly half of all states (24 states) had 5,000 or more jobs that could be pegged to NIH investment, led by California (63,196), New York (33,193 jobs), Massachusetts (34,598 jobs), and Texas (25,878 jobs).[17]

The Human Genome Project (HGP) is another example of how NIH funding leads to large and widespread benefits for the Nation. According to the 2011 report written by Battelle, *Economic Impact of the Human Genome Project*, the HGP directly and indirectly generated $796 billion in economic output between 1988 and 2010.[18] In 2010 alone, the HGP directly and indirectly supported more than 300,000 jobs. The HGP has transformed medical research, providing systematic approaches for discovering genes and cellular pathways that underlie diseases.

Analyses focusing on the direct and indirect linkages between NIH and economic activity also support NIH's role as an "economic engine." Public funding for research and development in general—and for NIH in particular—is a complement, not a substitute or an alternative, to private investment. Studies show that private industry builds on the basic, fundamental discoveries made possible by publicly supported life sciences research—discoveries that catalyze rather than stifle innovation.

[17] *An Economic Engine: NIH Research, Employment and the Future of the Medical Innovation Sector*

[18] *Battelle Technology Partnership Practice "Economic Impact of the Human Genome Project" 2011.* *http://battelle.org/docs/default-document-library/economic_impact_of_the_human_genome_project.pdf?sfvrsn=2*

Securing an AIDS-free Generation

AIDS remains a global scourge affecting people in nearly every country worldwide. According to UNAIDS, in 2010, more than 34 million people worldwide were estimated to be living with HIV/AIDS; 2.7 million were newly infected; and 1.8 million people died of AIDS-related illnesses. The CDC reports that in the U.S., more than 1.2 million people are estimated to be HIV-infected, and approximately 50,000 new infections occur per year; the incidence of new infections has not declined for more than a decade. At the same time, tremendous progress in treatment and prevention research, supported by NIH, are enabling the world to imagine achieving an AIDS-free generation.

A promising new area is the study of treatment strategies as a method to prevent new HIV infections. In 2011, an NIH-supported study demonstrated a 96 percent reduction in HIV transmission to uninfected partners if antiretroviral treatment was started earlier in the HIV-infected partners. This study (HPTN 052), conducted by the NIH-supported HIV Prevention Trials Network, was selected as the 2011 "Breakthrough of the Year" by the journal *Science*. An innovative prevention strategy known as "seek, test, and treat" is currently being evaluated domestically to determine the impact at the community level of increased testing among high-risk, hard-to-reach populations with immediate referral to treatment.

The best long-term hope for controlling the AIDS pandemic is the development of safe, effective, and affordable AIDS vaccines that can be used in combination with other prevention strategies. To date, NIH has supported 125 vaccine trials involving 80 different products and 26 adjuvants. The "Thai trial" (RV144) was the first HIV vaccine trial to demonstrate a modest reduction in the risk of HIV transmission (31.2 percent efficacy). Another recent advance in HIV vaccine research at the NIH focuses on broadly neutralizing HIV antibodies; these studies are providing information that is critical for rational vaccine design.

Priorities for future HIV/AIDS research at the NIH include follow up studies of the Thai vaccine and studies to identify and evaluate new candidate vaccines to induce and optimize immune responses. NIH is also expanding research into neutralizing antibodies to be applied in vaccine, passive infusion or gene transfer approaches. Another research priority for NIAID is to identify where HIV hides, known as the HIV reservoir, determine how these hideouts are established and maintained, and to develop strategies to control and eliminate them. Continued studies of antiretroviral drugs and microbicides as treatments or prevention strategies are needed as well. NIH also continues to support research to understand better how to change the risk behaviors that lead to HIV infection and disease progression, as well as how to maintain protective behaviors once they are adopted. The recent advances and future research supported by the NIH are essential to the achievement of an AIDS-free generation.

Analyses conducted by various expert groups, including the National Bureau of Economic Research and the Health Economics Research Group at Rand Europe, provide evidence of the positive effects of public funding on private investment: according to one analysis, when added to the stock of public funding for research and development, every additional dollar induces an additional twenty-seven cents in private investment; according to another, a dollar of NIH support for research leads to thirty-two cents in medical research funding from private sources. Public funding for biomedical research in general and for NIH in particular has generated multiple benefits—including a life sciences industry that ranks among the strongest performers

in the U.S. economy. This industry accounts for an estimated $69 billion in economic activity—making it one of the American economy's most vital sectors.[19]

Strengthening American Competitiveness

Public investment in biomedical research through NIH triggers complementary private investments, creates and sustains jobs, and produces real, measurable benefits to the American economy. At a time when global competition in the life sciences is intensifying, the demonstrable, proven value of the public's investment in NIH offers a reliable strategic advantage in any quest to secure and enhance the Nation's global leadership in scientific efforts to advance human health.

In the face of growing global competition, sustained investment in scientific innovation and the scientific workforce in the U.S. will continue to propel scientific discovery. Countries such as China and India are increasingly investing resources into biomedical science and technology. As reported in *Science and Engineering Indicators 2012,* the National Science Board observed that "[I]n most broad aspects of science and technology activities, the U.S. continues to maintain a position of leadership. But it has experienced a gradual erosion of its position in many specific areas. Two contributing developments to this erosion of its position are the rapid increase in a broad range of Asian science and technology capabilities outside of Japan and the effects of European Union efforts to boost its relative competitiveness in research and development, innovation, and high technology." [20] Added to this is the fact that federal investment in the U.S. has been declining: during the space race of the 1960s, the U.S. dedicated 17 percent of its budget to research and development; in 2008, total outlays in this crucial category were just over nine percent of the federal budget.[21] According to the Organization for Economic Cooperation and Development, in 2008, including both public and private sources, the U.S. invested 2.8 percent of its gross domestic product (GDP) in research and development—less than Israel, Japan, Korea, Sweden and Switzerland.

The linkages between publicly funded biomedical research and advancements in human health are well established and recognized and continue to supply the ultimate rationale for NIH as an agency dedicated to the public good of health.

[19] *An Economic Engine: NIH Research, Employment and the Future of the Medical Innovation Sector*
[20] *National Science Board, Science and Engineering Indicators 2012, Overview, p. 3*
[21] *American Association for the Advancement of Science, "AAAS Report XXXV: Research and Development FY2011, 2010, available at http://www.aaas.org/spp/rd/rdreport2011/*

NATIONAL INSTITUTES OF HEALATH
FY 2014 Congressional Justification

Impact of Budget Level on Performance
(Dollars in Millions, except where noted)

Programs and Measures	FY 2012 Actual	FY 2014 PB	FY 2014 +/- FY 2012
Research Project Grants	$16,550	$16,932	2.3%
Competing Average Cost (in thousands)[1]	$421	$456	8.4%
Number of Competing Awards (whole number)	8,986	10,269	14.3%
Estimated Competing RPG Success Rate: Absolute Rate	18%	19%	1.7%
Research Centers	$3,040	$2,846	-6.4%
Other Research	$1,808	$1,866	3.2%
Training Programs	$762	$776	1.8%
Research & Development Contracts	$2,911	$3,030	4.1%
Intramural Research	$3,429	$3,495	1.9%
Research Management and Support	$1,530	$1,550	1.3%
Common Fund (non-add)	*$545*	*$573*	*(5.1%)*
Buildings and Facilities Appropriation	$125	$126	0.6%
Other Mechanisms[2]	$704	$710	0.8%
Total, Program Level[3]	**$30,860**	**$31,331**	**1.5%**

[1] The estimated average cost of new/competing RPGs for FY 2014 appears to increase by over eight percent compared to FY 2012 due to the expected award about 100 very large new grants in FY 2014. Without those outliers the projected FY 2014 average cost would be only slightly higher than FY 2012.

[2] Includes Office of the Director-Other, Facilities funds for NCI-Frederick, Interior Superfund appropriation, and National Library of Medicine (NLM) Program Evaluation.

[3] Includes Labor/HHS Budget Authority, Interior Superfund Appropriation, Type 1 Diabetes mandatory funding and NLM Program Evaluation.

Overview of Performance

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. Investments in basic biomedical and behavioral research make it possible to understand the causes of disease onset and progression, design preventive interventions, develop better diagnostics, and discover new treatments and cures. Realizing the benefits of fundamental biomedical discoveries depends on the translation of that knowledge into the development of new diagnostics, therapeutics, and preventive measures to improve health. Investments in translational research are leading to the identification of new targets and pathways for the development of new therapeutics.

The FY 2014 NIH Budget Request reflects the agency's long-standing commitment to invest strategically using performance-based analysis, as emphasized in the GPRA Modernization Act of 2010 (P.L. 111-352). Through the continuous evaluation and strategic management of its research portfolio, the NIH focuses on funding research that shows the greatest promise for improving the overall health of the American people. In addition, NIH continually seeks to identify and address high priority scientific opportunities and emerging public health needs. By managing its research portfolio to support key research priorities, NIH ensures the most effective use of funds to achieve the greatest impact on the health and welfare of the Nation. In particular, NIH's strong peer review process, site visits, performance monitoring, program evaluation and performance-based contracting enable the agency to ensure that its investments generate results for the American people.

NIH strives to achieve transparency and accountability by regularly reporting results, achievements, and the impact of its activities. To increase transparency and promote effective use of resources, NIH will begin reporting the amount of indirect costs paid per grant on its Research Portfolio Online Reporting Tools website (NIH RePORT) by October 1, 2013. The agency supports a wide spectrum of biomedical and behavioral research and engages in a full range of activities that enable research, its management, and the communication of research results. Because of this diversity and complexity, NIH uses a set of performance measures that is representative of its activities and is useful for tracking progress in achieving performance priorities. This representative approach has helped NIH to share progress of its performance priorities with HHS, the rest of the Executive Branch, the Congress, and the public.

The NIH performance measures reflect the agency's overall goals to advance basic biomedical and behavioral science, support translational research, and enhance the development of human capital and strengthen the scientific workforce. The measures also support the goals and objectives of the HHS Strategic Plan 2010-2015. In particular, the NIH substantially contributes to the HHS Strategic Goal 2 – Advance Scientific Knowledge and Innovation (Objective A: Accelerate the process of scientific discovery to improve patient care). For example, in FY 2014, the NIH will support research with the goals of: (1) making freely available to researchers the results of 400 high-throughput biological assays, screened against a library of 300,000 unique compounds that are expected to provide a scientific resource that will accelerate the discovery of protein functions that control critical processes such as development, aging, and disease; and (2)

identifying and characterizing two molecular pathways of potential clinical significance that may serve as the basis for discovering new medications for preventing and treating asthma exacerbations.

Moreover, in support of the President's goal of strengthening and modernizing the U.S. health care system and the HHS Strategic Goal 1 – Strengthen Health Care (Objective C: Emphasize primary and preventive care linked with community prevention services), the NIH will continue to support research to identify three key factors influencing the scaling up of research-tested interventions across large networks of services systems such as primary care, specialty care and community practice.

Performance Management

Performance management at NIH is an integrated and collaborative process to ensure that the agency is achieving its mission to conduct and support research to improve public health. At the agency level, the NIH Director sets priorities, monitors performance, and reviews results across the 27 Institutes and Centers (ICs) and the Office of the Director (OD). The OD is the central office that is responsible for setting policy for NIH and for planning, managing, and coordinating the programs and activities of all NIH components. The NIH Director provides leadership to the ICs and helps identify needs and opportunities, especially for efforts that involve multiple ICs. Each IC and OD office carries out priority setting, performance monitoring, progress reviews, and makes adjustments based on progress achieved in their respective areas of science. In addition to the performance management processes that occur for the NIH research program, there are equivalent processes for administrative management functions.

The NIH performance framework includes: (1) priority setting with input from key stakeholders; (2) implementation and management of activities that support priorities; (3) monitoring and assessment of progress, and identification of successes and challenges; (4) oversight by IC leadership and OD office directors in assessing overall progress towards priorities and identification of best practices, appropriate next steps, and corrective actions (as needed); (5) incorporation of regular feedback from IC and OD office leadership to enhance activities; (6) regular reviews of priorities, progress, and outcomes by the NIH Director and IC Directors; and (7) regular review of performance and priorities by external expert review groups including grant peer review groups, Advisory Councils, and ad hoc working groups.

Qualitative and quantitative information is used to monitor progress and help to identify successes as well as obstacles in achieving short- and long-term goals. Supporting high performing research is a process of adapting to new developments or newly identified barriers, or shifting resources to pursue promising unanticipated results that may provide critical new information. Moreover, the impact of research may not be immediately known and may depend on additional development or on advances in other fields. Despite these challenges, NIH leadership is able to manage performance effectively by using the best available information to assess progress toward achieving priorities and making appropriate adjustments.

Research is an inherently collaborative endeavor and partnerships are crucial to achieving scientific research outcomes. The role of the extramural research community (the scientists at

universities and hospitals across the country and around the world) as NIH's partner in research is well known. However, of increasing importance are partnerships with private companies, not-for-profit institutions, non-governmental organizations, other Federal agencies, and state and foreign governments. Joint research and training activities and other exchanges with such groups increase the leverage of NIH resources and support vibrant partnerships to help the NIH achieve its mission. Moreover, such partnerships facilitate valuable information feedback loops that identify emerging needs, suggest important new research questions, and otherwise inform priority setting. Partnerships also provide access to populations that are essential to advancing knowledge.

All scientific research carried out through NIH support is subjected to a rigorous and consistently applied review processes. For example, the Extramural Research Program, which oversees the largest category of NIH-funded research, utilizes two levels of peer review. The first level consists of chartered scientific review groups composed of outside experts in particular scientific disciplines. The second level is the National Advisory Councils of the various Institutes. For the Intramural Research Program, the progress of individual scientists and their laboratories is evaluated once every four years by Boards of Scientific Counselors composed of external experts. These reviews enable ongoing assessments of all intramural labs and the accomplishments of the scientists who contribute to them. It is through this well-honed system of peer review that the NIH can maintain its focus on supporting research of the highest possible quality.

The NIH approach to performance management is undergirded by the NIH Governance Structure. That structure includes the NIH Steering Committee[22] and five standing Working Groups.[23] Ad hoc working groups are established, as needed, to address emerging issues. The premise of the structure is that shared governance, which depends on the active participation of the IC Directors with the NIH Director, will foster the collaborative identification of corporate issues and a transparent decision-making process. With active participation by the IC Directors in NIH-wide governance, the NIH can maximize its perspective and expertise in the development and oversight of policies common to the NIH and its ICs. Through the governance process, corporate decisions are made; these may be long-term and strategic (e.g., facilities planning, budget strategy, research policy direction) or short-term and tactical (e.g., stipend levels, resource allocations and compliance oversight). This process does not include issues related to the setting of scientific priorities which is reserved for meetings of all IC Directors. The NIH Director meets with the IC Directors on a bi-weekly basis, and scientific initiatives are discussed as well as major management issues that affect the agency. In addition, scientists — from within and outside the agency — are invited to present on new or emerging research opportunities. The NIH Director stays informed of priorities through regular, individual meetings with IC and OD Office Directors. Similarly, the IC Directors monitor performance through regular meetings with the Division Directors and Scientific/Clinical Directors in their respective ICs. Based on these reviews, leadership and their staff take appropriate actions to support research activities. For

[22] *The NIH Steering Committee is composed of the NIH Director, Deputy Director (ex-officio), the Directors of NCI, NHLBI, and NIAID, as well as a balance of Directors from the smaller and medium sized institutes.*
[23] *The five standing working groups are: Extramural Activities, Intramural, Information Technology, Facilities, and Management and Budget.*

example, the reviews may lead to the development of new award programs for early career researchers, the development of new funding announcements for promising research areas, or new collaborations across NIH and/or with other Federal and non-Federal partners. The NIH Director and senior leadership receive regular updates on the progress of the priorities, provide feedback, and incorporate the latest information into the NIH's overall planning and management efforts. This constant feedback loop enables NIH to make critical adjustments periodically to align activities and target resources in support of its research priorities.

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Budget by HHS Strategic Goal[1]
(Dollars in Millions)

HHS Strategic Goals	FY 2012 Actual	FY 2013 CR	FY 2014 PB
1. *Strengthen Health Care*	**$683**	**$686**	**$901**
1.A Make coverage more secure for those who have insurance	0	0	0
1.B Improve health care quality and patient safety and extend affordable coverage to the uninsured	0	0	0
1.C Emphasize primary & preventative care link with community prevention services	683	686	901
1.D Reduce growth of health care costs while promoting high-value effective care	0	0	0
1.E Ensure access to quality culturally competent care for vulnerable populations	0	0	0
1.F Promote the adoption and meaningful use of health information technology	0	0	0
2. *Advance Scientific Knowledge & Innovation*	**$28,199**	**$28,467**	**$28,499**
2.A Accelerate the process of scientific discovery to improve patient care	28,199	28,467	28,499
2.B Foster innovation at HHS to create shared solutions	0	0	
2.C Invest in the regulatory sciences to improve food & medical product safety	0	0	0
2.D Increase our understanding of what works in public health and human services	0	0	0
3. *Advance the Health, Safety, and Well-Being of American People*	**$0**	**$0**	**$0**
3.A Promote the csafety, well-being, resilience and healthy development of children and youth safety	0	0	0
3.B Promote economic & social well-being for individuals, families and communities	0	0	0
3.C Improve the accessibility and quality of supportive services for people with disabilities and older adults	0	0	0
3.D Promote prevention and wellness	0	0	0
3.E Reduce the occurrence of infectious diseases	0	0	0
3.F Protect Americans' health and safety during emergencies, and foster resilience in response to emergencies	0	0	0
4. *Increase Efficiency, Transparency, and Accountability of HHS Programs*	**$1,939**	**$1,771**	**$1,786**
4.A Ensure program integrity and responsible stewardship of resources	1,939	1,771	1,786
4.B Fight fraud and work to eliminate improper payments	0	0	0
4.C Use HHS data to improve American health and well-being of the American people	0	0	0
4.D Improve HHS environmental, energy, and economic performance to promote sustainability	0	0	0
5. *Strengthen the Nation's Health & Human Service Infrastructure & Workforce*	**$39**	**$133**	**$145**
5.A Invest in HHS workforce to meet America's health and human service needs today & tomorrow	39	133	145
5.B Ensure that the Nation's health care workforce meets increased demands.	0	0	0
5.C Enhance the ability of the public health workforce to improve health at home and abroad	0	0	0
5.D Strengthen the Nation's human service workforce	0	0	0
5.E Improve national, State & local surveillance and epidemiology capacity	0	0	0
TOTAL	**$30,860**	**$31,057**	**$31,331**

[1] NIH does not have an account or collection of accounts dedicated to program management. To allocate costs for program management, the Research Management and Support (RMS) line item was selected from the NIH mechanism display and Office of the Director Operations, a line item in the appropriation for the Office of the Director. Methodology used to allocate NIH total budget to HHS strategic goals and objectives was refined to ensure programmatic alignment. The totals were reduced by the direct costs of the performance measures that are funded through RMS or OD operations. This calculated level for Program Management was allocated across GPRA measures and the unsampled program on a pro-rata basis.

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Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2012 Actual		FY 2013 Annualized Continuing Resolution[2]		FY 2014 President's Budget		Change FY 2014 +/- FY 2012	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	25,631	$11,908,428	25,052	$11,838,330	24,566	$11,365,357	-1,065	-$543,071
Administrative Supplements	*(1,542)*	191,553	*(1,420)*	*(156,572)*	*(1,341)*	146,780	*(-201)*	-44,773
Competing:								
Renewal	1,995	955,538	2,140	985,424	2,322	1,378,655	327	423,117
New	6,956	2,817,956	7,426	3,009,507	7,915	3,296,940	959	478,985
Supplements	35	8,753	34	8,834	32	9,608	-3	855
Competing	8,986	$3,782,245	9,600	$4,003,765	10,269	$4,685,203	1,283	$902,958
Subtotal, RPGs	34,617	$15,882,227	34,652	$15,998,666	34,835	$16,197,340	218	$315,113
SBIR/STTR	1,642	$668,260	1,691	$692,214	1,775	$735,051	133	$66,791
Research Project Grants	36,259	$16,550,487	36,343	$16,690,880	36,610	$16,932,391	351	$381,904
Research Centers:								
Specialized/Comprehensive	1,216	$2,282,818	1,204	$2,204,970	1,158	$2,099,836	-58	-$182,983
Clinical Research	65	398,456	65	398,473	65	399,581		1,125
Biotechnology	100	160,608	90	153,880	90	154,735	-10	-5,873
Comparative Medicine	50	139,499	47	139,506	47	139,308	-3	-191
Research Centers in Minority Institutions	22	58,994	20	54,945	20	52,405	-2	-6,589
Research Centers	1,453	$3,040,375	1,426	$2,951,773	1,380	$2,845,864	-73	-$194,511
Other Research:								
Research Careers	3,843	$631,601	3,915	$643,963	3,867	$639,812	24	$8,211
Cancer Education	93	33,373	93	33,520	93	33,520		147
Cooperative Clinical Research	392	430,353	375	425,888	412	430,096	20	-257
Biomedical Research Support	115	67,917	97	68,567	94	66,860	-21	-1,057
Minority Biomedical Research Support	347	110,880	350	111,615	350	111,615	3	735
Other	1,706	534,015	1,763	579,827	1,733	584,474	27	50,459
Other Research	6,496	$1,808,138	6,593	$1,863,380	6,549	$1,866,377	53	$58,239
Total Research Grants	44,208	$21,398,999	44,362	$21,506,034	44,539	$21,644,632	331	$245,633
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	3,045	$129,715	3,095	$132,267	3,106	$135,257	61	$5,542
Institutional Awards	13,260	632,219	13,279	633,808	13,091	640,718	-169	8,499
Total Research Training	16,305	$761,934	16,374	$766,075	16,197	$775,975	-108	$14,041
Research & Development Contracts	2,492	$2,910,956	2,483	$2,953,044	2,492	$3,029,833		$118,877
(SBIR/STTR) (non-add)	*(127)*	*(57,175)*	*(120)*	*(63,002)*	*(112)*	*(60,244)*	*(-15)*	*(3,069)*
Intramural Research		$3,429,070		$3,457,139		$3,495,298		$66,228
Research Management and Support		1,530,359		1,540,512		1,549,871		19,512
Office of the Director - Appropriation [3]		*($1,457,168)*		*($1,466,320)*		*($1,473,398)*		*($16,230)*
Office of the Director - Other		608,713		612,620		614,136		5,423
ORIP & SEPA (non-add) [3,4]		*(303,525)*		*(305,435)*		*(286,314)*		*(-17,211)*
Common Fund (non-add) [3]		*(544,930)*		*(548,265)*		*(572,948)*		*(28,018)*
Buildings and Facilities [5]		133,228		134,031		134,031		803
Appropriation		*(125,308)*		*(126,111)*		*(126,111)*		*(803)*
Type 1 Diabetes [6]		-150,000		-150,000		-150,000		
Subtotal, Labor/HHS Budget Authority		**$30,623,259**		**$30,819,454**		**$31,093,776**		**$470,517**
Interior Appropriation for Superfund Res.		78,928		79,411		79,411		483
Total, NIH Discretionary B.A.		**$30,702,187**		**$30,898,865**		**$31,173,187**		**$471,000**
Type 1 Diabetes		150,000		150,000		150,000		
Total, NIH Budget Authority		**$30,852,187**		**$31,048,865**		**$31,323,187**		**$471,000**
NLM Program Evaluation		8,200		8,250		8,200		
Total, Program Level		**$30,860,387**		**$31,057,115**		**$31,331,387**		**$471,000**

1 All numbers in italics and brackets are non-add. FY 2012 and FY 2013 figures are shown on comparable basis to FY 2014 to reflect the NCBI and PA proposal; FY 2012 also reflects Secretary's Transfers for Ryan White AIDS and NIH Alzheimer's disease activities.

[2]Annualized CR level with 0.612 percent across the board increase.

[3]Number of grants and dollars for the Common Fund, ORIP and SEPA components of OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriations also is noted as a non-add since these funds are accounted for und

[4]Includes only ORIP and not SEPA in FY 2014 due to proposed government-wide Science, Technology, Engineering, and Mathematics education reorganization plan.

[5]Includes B&F appropriation plus facilities dollars appropriated to NCI.

[6]Number of grants and dollars for mandatory Type 1 Diabetes are distributed by mechanism above; therefore, Type 1 Diabetes amount is deducted to provide subtotals only for the Labor/ HHS Budget Authority.