DEPARTMENT of HEALTH and HUMAN SERVICES

FISCAL YEAR 2015

NATIONAL INSTITUTES OF HEALTH - Volume I

Overview

Justification of Estimates for Appropriations Committees

As the Director of the National Institutes of Health (NIH), I am pleased to present the Congressional Justification of the NIH fiscal year (FY) 2015 budget request. This budget request for $30.362 billion total program level reflects the President's and the Secretary's commitment to improve the health of all Americans and maintain the country's leadership in the biomedical sciences. The request highlights pioneering research investments that will increase understanding of underlying disease causes and spur development of innovative diagnostics, treatments, and preventive approaches to improve health. With this budget request, NIH will be able to recruit and support a talented and diverse workforce to bring new insights to our understanding of biology and to advance the translation of these insights into improved health for all.

As stewards of the Nation's principal investment in biomedical science, NIH engages in a dynamic, multidimensional process for determining how best to distribute its resources. In order to address the public health needs of today while preparing ourselves for any emerging and unexpected needs of tomorrow, NIH works diligently to plan both short- and long-term research investments. Such planning involves careful balancing of basic science and applied studies that will translate basic knowledge into new strategies for enhancing health and reducing illness and disability. The strength of NIH's approach is evidenced by the extraordinary number of innovative discoveries in biomedical science that have been produced through NIH-funded research.

NIH investments in cutting edge technology will also continue to drive economic development in the United States. For example, innovative advances in genomics and imaging technologies, as well as computing power for working with big data, will stimulate new businesses while also catalyzing advances in innumerable scientific fields, ranging from traumatic brain injury and Alzheimer's disease to advances in diagnosis and treatment for cancer, diabetes, and autism. Overall, the FY 2015 budget request will enable NIH to continue its investments in groundbreaking research, scientific workforce training, and technologies of the future. In addition, NIH is seeking additional funding for two high priority initiatives that promise to generate significant advances in biomedical research - the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative and the Big Data to Knowledge (BD2K) Initiative. This budget request provides the flexibility for NIH to prioritize research to reduce disease burden, increase disease prevention, and respond to emerging public health needs.

I look forward to the opportunity to discuss this FY 2015 budget request and NIH's plans for the future.

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

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FY 2015 Budget

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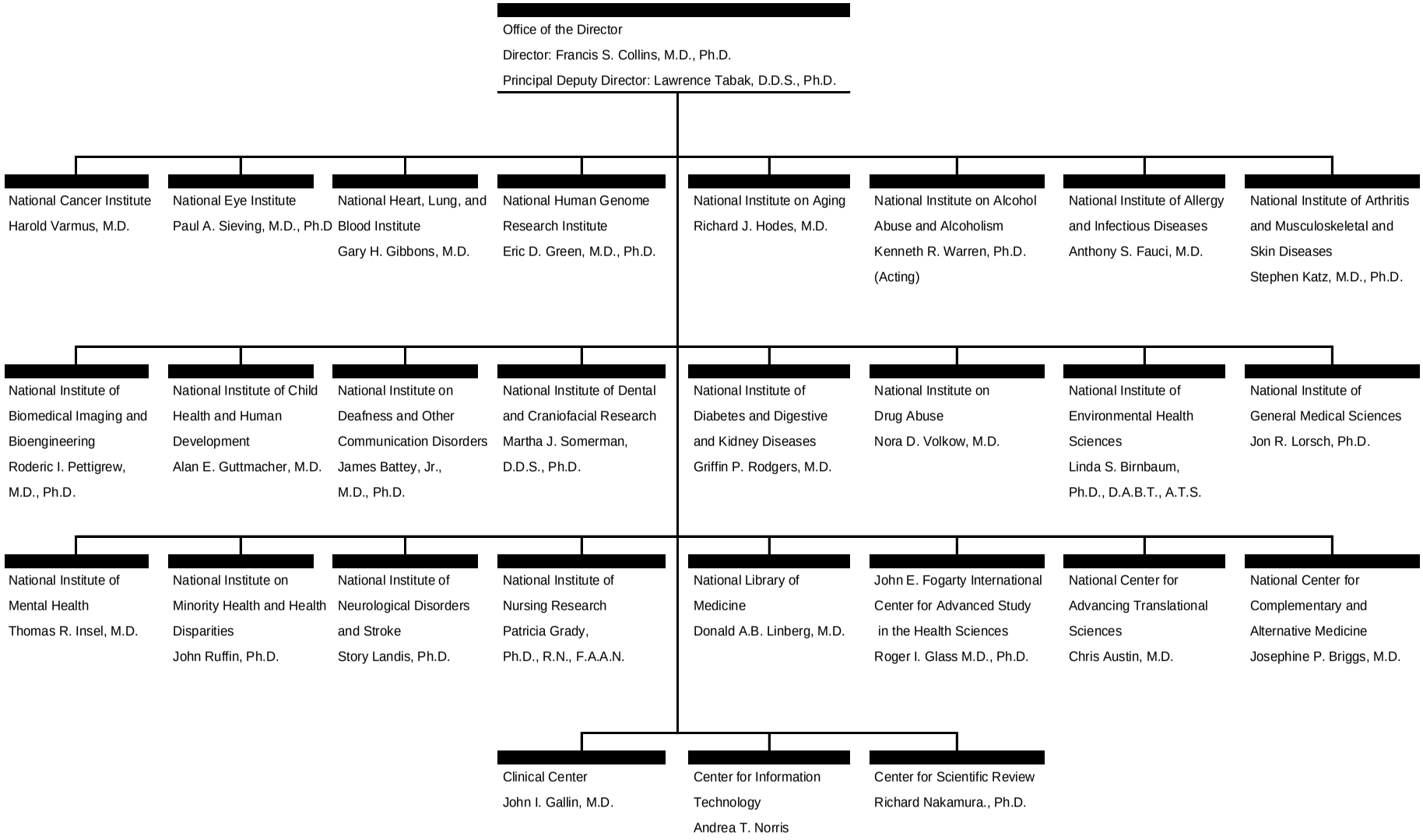
Executive Summary

Department of Health and Human Services
National Institutes of Health

Executive Summary

National Institutes of Health



FY 2015 Budget Request
National Institutes of Health

Introduction and Mission

The mission of the National Institutes of Health (NIH) 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 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 improved health. A significant and enduring investment by NIH in basic research today assures the breakthroughs in the health care of tomorrow. This robust research enterprise depends upon NIH's ability to recruit and retain the Nation's brightest minds into successful scientific careers. With continued support, NIH contributes significantly to the economic engine that drives American competitiveness in science and technology and will realize a Nation in which all Americans enjoy long healthy lives.

National Institutes of Health
FY 2015 Congressional Justification

All Purpose Table
(Dollars in Thousands)

	FY 2013 Actual[1]	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 Request +/- FY 2014 Enacted
Labor/HHS Discretionary Budget Authority	**$28,926,041**	**$29,926,104**	**$30,126,104**	**$200,000**
Interior Budget Authority	74,871	77,349	77,349	0
Total Discretionary Budget Authority	**$29,000,912**	**$30,003,453**	**$30,203,453**	**$200,000**
Mandatory Type 1 Diabetes Research	142,350	139,200	150,000	10,800
Total Budget Authority	$29,143,262	$30,142,653	$30,353,453	$210,800
NIH Program Level[2]	**$29,151,462**	**$30,150,853**	**$30,361,653**	**$210,800**
Number of Competing RPGs	*8,234*	*8,997*	*9,326*	*329*
Total Number of RPGs	*34,840*	*34,213*	*34,197*	*(16)*
FTEs	*18,234*	*18,234*	*18,234*	*0*

[1] Includes effect of sequestration and transfers.

[2] Includes NLM Program Evaluation of $8.20 million in FY 2013, FY 2014 and FY 2015.

FY 2015 Budget Request
National Institutes of Health

OVERVIEW OF BUDGET REQUEST

Total Budget Request
(Dollars in Millions)

	FY 2014 Enacted	FY 2015 President's Budget
Total Program Level [1]	$30,151	$30,362
Change from FY 2014 Enacted: Dollars	--	$211
Change from FY 2014 Enacted: Percent	--	0.7%

[1] 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 $30.362 billion for fiscal year (FY) 2015, $211 million above the FY 2014 level. This funding will enable NIH to sustain the pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Investment in NIH provides the Nation with a unique resource–a scientific agency devoted to the creation of a knowledge base needed to conquer the most devastating human diseases and disabilities. The promise of NIH is that someday all people will be able to lead long and healthy lives.

In striving to fulfill this promise, the 27 Institutes and Centers that comprise NIH work together with the NIH Office of the Director to support the science needed to develop new ways to prevent, diagnose, and treat the diseases and disorders that cause the greatest burdens to society. For example, in large part due to advances supported by NIH, deaths from heart disease have fallen by more than 60 percent since 1970[1]. In addition to focusing on those diseases with the greatest burden, NIH also conducts research on rare and neglected conditions that would otherwise go unaddressed. For many suffering from these conditions, NIH is their only hope. And knowledge gained about rare diseases often has important implications for more common conditions as well. For example, in 2012, NIH scientists identified a genetic mutation that causes cold temperatures to trigger an allergic reaction–a condition called cold urticaria. In addition to informing efforts to find a cure for this rare condition, this finding provided important information on how the immune system functions.

[1] *Calculated from Health, United States, 2011: with Special Feature on Socioeconomic Status and Health, http://www.cdc.gov/nchs/data/hus/hus11.pdf*

NIH research results not only help generate new approaches to diagnose and treat known diseases, but also help to address emerging threats. In the mid-1980s, a diagnosis of AIDS was considered a death sentence. Yet, in large part because of what was already known through basic research on the immune system and retroviruses, not only was the cause of AIDS quickly identified, but effective strategies toward its prevention and treatment were being pursued in short order. The result has been that in 30 years' time we have moved from contemplating a decrease in world population due to AIDS to designing approaches to end the epidemic.

Science moves at an unpredictable pace and not all areas of inquiry progress in the same way. In establishing funding priorities, NIH must maintain strong, diverse investments in basic science; the development of effective diagnostics, treatments, and preventive measures for both common and rare diseases; and the need to sustain a vital and cutting-edge workforce and scientific infrastructure. This approach allows NIH to capitalize on scientific opportunities as they emerge, as well as maintaining the flexibility to respond to urgent public health needs.

In addition to the base Budget request, the FY 2015 President's Budget contains a proposed Opportunity, Growth, and Security Initiative to support the President's priorities to grow the economy and create opportunities. This Initiative includes $970 million to restore NIH to the level proposed in the FY 2014 President's Budget ($31.3 billion). These funds, which would be used to increase the number of new grants and provide additional resources for signature biomedical research activities, are described in the Overall Appropriations section under Narrative by Activity.

In FY 2015, NIH will focus on the following priority themes:

1. Today's Basic Science for Tomorrow's Breakthroughs
2. Precision Medicine
3. Big Opportunities in Big Data
4. Nurturing Talent and Innovation

By pursuing these priorities, NIH will drive the engine of discovery, innovation, and improved health. NIH is uniquely poised to pursue the priorities because of our public responsibility, resources, or willingness to pursue areas and diseases which others are not.

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

NIH is the largest funder of basic biomedical research in the world. By funding basic research, NIH provides the foundational knowledge of the mechanisms of biology and behavior that are necessary to understand the causes of disease onset and progression, identify risk factors and biological markers that allow for better diagnostics, and develop new cures and preventive treatments. Often, this foundational knowledge is built in small increments that eventually lead to major breakthroughs, but it also provides the necessary groundwork for tackling newly emerging infectious diseases or complex chronic diseases that are rapidly increasing in burden. Therefore, support of a broad basic research portfolio is essential in fulfilling NIH's mission of addressing the public health challenges of both today and the future.

Basic research results advance not only knowledge of a specific disease or condition but also build the tools that will help advance understanding in many other areas. For example, several NIH-supported researchers have developed and are refining a new technology called CRISPR (clustered regularly interspaced short palindromic repeats), which enables scientists to target genes for deletion, addition, activation, or suppression with such specificity that it amounts to performing their own genetic microsurgery. Using this system, researchers have altered DNA in human cells, rats, mice, zebrafish, bacteria, fruit flies, yeast, nematodes, and crops. This method arose from basic research in an area unrelated to gene editing, and its wide-ranging applicability makes the technology potentially valuable for numerous purposes, including treatment of genetic diseases.

NIH also supports key collaborations in basic research. The Knockout Mouse Phenotyping Program (KOMP2), supported by NIH in cooperation with the European Union, Wellcome Trust, Canada, and the Texas Enterprise fund, is systematically producing mice that have specific traits that are useful as models for understanding how genes work and how they are related to diseases. The Library of Integrated Network-based Cellular Signatures (LINCS), created by NIH-funded researchers, is providing a blueprint of how the basic parts of cells, including genes, proteins and other molecules, work together and are maintained not only in health but also in how they respond to disease. The Genotype Tissue Expression (GTEx) Program is illuminating how genes work in different tissues and in different people; and the 1000 Genomes project is supporting the development of cost-effective and high-throughput genome sequencing methods for protein coding regions of the genome to help enhance our understanding of how proteins are made. The results of the Human Genome Project revealed that the protein-coding portions of DNA account for only about 1.5 percent of the genetic material found in humans, while the purpose of the other 98.5 percent remained unknown. To unravel this mystery, NIH initiated the Encyclopedia of DNA Elements (ENCODE) project to identify all functional elements of the human genome sequence, including those that act through the production of protein and RNA, as well as regulatory elements that control gene activity of cells. Through this herculean effort, researchers have now linked more than 80 percent of the human genome sequence to a specific biological function, and mapped more than 4 million regulatory regions where proteins specifically interact with the DNA–representing a major advance in the emerging science of "epigenomics." This information is freely available online in a resource that can be accessed by all researchers to use in further studies.

Numerous other basic research projects funded by NIH are producing findings that are increasing our understanding of disease processes or new ways of treating diseases or conditions. For example, researchers funded by NIH's National Institute of General Medical Sciences (NIGMS) have achieved major advances in understanding the process of protein production from RNA by providing the means to visualize the molecular machinery that initiates this process. The National Eye Institute (NEI) has funded research that has identified small fragments of proteins in the cornea that fight infections and have the potential to be manufactured as a new class of low-cost, non-toxic antibiotics. Researchers funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) are generating significant data to help understand the role of the immune system in skeletal muscle regeneration after injury. These are only a few examples of the knowledge, tools, and resources being developed through NIH's funding of basic research.

The BRAIN Initiative[SM]

The complexity of the human brain was once thought to be beyond understanding–the brain comprises nearly 100 billion cells that make an astounding 100 trillion connections. Current state-of-the-art imaging can provide mostly a static picture of brain activity, and electrodes can control and record electrical activity from single and small groups of neurons in specific locations, but a leap in scientific understanding and technological capability is needed in order to map entire brain circuits. Leveraging investments and diverse expertise from private foundations, industry, and other government agencies, the goal of the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative is to accelerate the development and application of next-generation tools to construct dynamic pictures of the brain that reveal how millions of brain cells and complex neural circuits interact in real time to produce the extraordinarily complex array of human behaviors.

The FY 2015 Budget includes $100 million for the BRAIN Initiative, an increase of $60 million over FY 2014, to ramp up activities in the second year. This bold multi-agency initiative requires ideas from the best scientists and engineers across many diverse disciplines and sectors. The BRAIN Initiative will build on the rapidly growing scientific foundation of neuroscience, genetics, physics, engineering, informatics, nanoscience, chemistry, mathematics, and technological advances of the past few decades to catalyze an interdisciplinary effort of unprecedented scope. Recent NIH-funded breakthroughs illustrate the transformative potential of technology to understand the brain's intricate architecture and complex functions:

- Imaging the brain: the Human Connectome Project has driven the development of increasingly sophisticated imaging tools, providing the first ever systematic map of the wiring diagram of nerve cells within the living human brain.
- Measuring brain activity: large-scale, multielectrode arrays are now being used in live animals to record from thousands of neurons simultaneously across different brain areas.
- Precision manipulation of brain activity: using optogenetic methods, scientists were able to switch depression-related behavior on and off in mice with flashes of an LED light, uncovering new insights into mechanisms of depression.
- Tracing the brain's connections: a ground-breaking technology called CLARITY takes a fully intact, opaque brain and transforms it into a clear, gel-based brain, allowing unprecedented 3-D visualization of molecular, cellular, and neuro-anatomic structure.

NIH has established a high-level working group of 18 external advisors, including three ex-officio members from the federal partner agencies, to define the goals of the BRAIN Initiative for NIH and develop a rigorous plan for achieving its scientific vision, including timetables, milestones, and cost estimates. The advisory group delivered an interim report detailing high-priority areas for FY 2014 funding in September of 2013, and will complete a final report with comprehensive recommendations in Summer 2014.

In accordance with recommendations issued by the working group, NIH's $40 million investment in the BRAIN Initiative in FY 2014 will focus on expanding and enhancing the arsenal of tools and technologies for unlocking the mysteries of the brain. The first wave of funding opportunities under the BRAIN Initiative were released on December 17: two focus on

developing methods for classifying and accessing diverse cells and circuits of the brain; three focus on developing and optimizing technologies for recording and modulating collections of cells that function together as a circuit; and one supports the formation of interdisciplinary teams of scientists to develop the next generation of non-invasive imaging technologies for human research.

Ultimately, application of the tools and technologies developed under the Brain Initiative will provide critical insight into brain circuitry and activity. This foundation of knowledge will help reveal the underlying pathophysiology in numerous brain disorders and may provide new therapeutic avenues to treat, cure, and even prevent neurological and psychiatric conditions, such as Alzheimer's disease, autism, epilepsy, schizophrenia, depression, chronic pain, addiction, post-traumatic stress disorder, and traumatic brain injury.

The Microbiome – New Insights into the Invisible Ecosystem in and on the Human Body and its Role in Health

The human body is host to trillions of microbes – outnumbering the body's cells by 10 to 1. Some of these bacteria, fungi, and viruses cause disease, but many are necessary for human health. To characterize these microbes and understand their influence on human health, the Human Microbiome Project (HMP) was launched by NIH in 2007. The first phase of the HMP, in volving the sequencing of microbial reference genomes from five areas of the body – the digestive tract, mouth, skin, nose and vagina – determined that more than 10,000 microbial species occupy the human body and that the microbiome provides more genes that contribute to human survival than the human genome itself (8 million vs. 22,000). A deeper understanding of the microbiome has led to numerous insights on how microbes keep us healthy and make us sick:

- The gut microbiome affects nutrition. NIH-funded researchers found that an acute form of malnutrition called kwashiorkor, which is common in the African nation of Malawi, is likely caused by both inadequate caloric intake and an improper balance of microbes in the gut. Even though all the kids in the study had a poor diet, the gut microbiome of healthy kids differed dramatically from those with kwashiorkor. The researchers concluded that children carrying the "bad" kwashiorkor gut microbes could not make the most efficient use of the Malawian diet, and thus ended up with malnutrition.

  The link between red meat consumption and heart disease may be influenced by how well gut microbes can break down carnitine, a compound found in red meat. The NIH-supported study showed that the gut microbes of meat eaters were more efficient at breaking down carnitine than those in non-meat eaters. In mice, the carnitine break-down product appeared to promote atherosclerosis, or clogging of the arteries. Therefore, a diet high in carnitine-containing red meat may shift our gut microbe composition to those that like carnitine, potentially making meat eaters even more susceptible to atherosclerosis.

  Gut microbes may also play significant roles in the development of immune system disorders. Type 1 diabetes is an autoimmune disease in which the body's own immune system attacks and destroys insulin-producing beta cells in the pancreas. NIH-funded researchers have reported that certain gut microbes protect against Type 1 diabetes in mice, essentially by blunting the immune system attack that causes Type 1 diabetes. The gut microbiome has been also been linked to arthritis. In a recent NIH-funded study, investigators found that 75% of people with new-onset, untreated rheumatoid arthritis had the bacterium *Prevotella copri* in their intestinal microbiome. When the team administered the bacteria to healthy mice, they developed more severe symptoms than the mice that had not received the bacteria, providing evidence for its potential harmful role in the development of rheumatoid arthritis.

Ongoing HMP projects are continuing to reveal the critical roles these diverse organisms play in a host of diseases and conditions, with specific projects focusing on obesity, asthma, kidney disease, Crohn's disease, ulcerative colitis, esophageal cancer, psoriasis, dermatitis, dental caries, periodontal disease, and a number of childhood disorders, such as pediatric abdominal pain, intestinal inflammation, and a severe condition in premature infants in which the intestine actually dies. Additionally, NIH-funded investigators are studying how the infant gut microbiome becomes established and what effect environmental changes, such as diet and antibiotic exposure, may have on "normal" gut microbiome early in life. The long-term objective of the HMP is to identify opportunities to improve human health through monitoring or manipulation of the human microbiome. The HMP investment by the Common Fund has stimulated microbiome research throughout NIH, and support by Institutes and Centers will exceed $30 million in FY 2015.

Theme 2: Precision Medicine

In addition to funding a diverse and robust portfolio in basic research, NIH also supports research focused on improving disease prevention, diagnosis and treatment. The primary goal of NIH translational and clinical research is to improve public health interventions and to provide the best available care for those who need it. Precision medicine refers to the tailoring of treatments to the individual characteristics of each patient. To do so, NIH seeks to understand human variability and identify individuals who differ in the susceptibility to a particular disease, in the trajectory of those diseases if they develop, or in response to a specific treatment. In this way, specific preventive or therapeutic interventions can be tailored–avoiding needless treatment and expense for those who will not benefit. Understanding the characteristics that make an individual more susceptible to a disease or disorder or identifying predictive markers for response to a particular treatment will also improve screening and allow for better implementation of interventions in any number of healthcare and community settings.

NIH undertakes the challenges of precision medicine through myriad strategies. A key cornerstone has been creating the infrastructure to enable such research. To do so, NIH partners with a multitude of public and private entities within public health to pursue varied approaches. For example, NIH's National Center for Advancing Translational Sciences (NCATS) works with the pharmaceutical industry, academia, and the U.S. Food and Drug Administration (FDA) to look for new uses of drugs that have been found to be safe in humans. And an exciting new venture between NIH and ten biopharmaceutical companies and several non-profit organizations aims to transform the current model for developing new diagnostics and treatments by working together to identify and validate biological targets of disease. Focusing first on pilot projects in the areas of Alzheimer's disease, type 2 diabetes, and the autoimmune disorders of rheumatoid arthritis and lupus, the ultimate goal of the Accelerating Medicines Partnership is to increase the number of new diagnostics and therapies for patients and to reduce the time and cost of their development.

The field of medicine is rapidly advancing, and these advances are leading to increased precision in the diagnosis and treatment of individuals. Along this path, recent NIH advances include using a revolutionary brain-computer interface to enable a patient who had been paralyzed for nearly 15 years to be able to control a robot arm to retrieve and drink from a thermos of coffee. An NIH-supported study on peanut allergy demonstrated that sublingual immunotherapy (SLIT), in which a small amount of the substance that causes the allergic reaction is placed under the tongue, successfully reduced an allergic reaction in 70 percent of participants in a randomized, controlled trial. And a recent study has shown that bariatric surgery can help control type 2 diabetes more effectively than intensive medical therapy alone (lifestyle counseling, weight management programs, frequent home glucose monitoring, and the use of diabetes medications), and can reduce the need for medications to lower glucose, harmful lipids, and blood pressure.

Tissue on a chip

The current drug development pipeline has significant bottlenecks, and the movement of basic research into clinical use is slower than desired. Animal models have been the gold standard for testing the safety and efficacy of new therapeutic compounds. However, more than 30 percent of medications have generally failed in human trials because they are determined to be toxic,

despite promising and expensive studies in animal models. To help streamline therapeutic development, NIH along with its partners, the Defense Advanced Research Projects Agency (DARPA) and FDA, embarked in 2012 on a bold, technology-driven initiative to improve the process for predicting whether drugs will be safe in humans. This tissue-on-a-chip research initiative is aimed at developing 3-D human tissue chips that accurately model the structure and function of human organs, such as the lung, liver, and heart.

NIH and DARPA have complementary but distinct goals for this collaboration. While DARPA's initiative focuses on engineering aspects, the NIH initiative focuses on how well these new technologies mimic the biology and pathophysiology of human organ systems. Led by NCATS, 15 NIH Institutes and Centers are assisting in the coordination of this cross-cutting trans-NIH program, and to date, 19 grants have been awarded. Research teams have begun to develop 3-D cellular microsystems that recreate the genomic diversity, disease complexity, and drug responses of approximately 10 different human organ systems, including the heart, lung, and nervous system. Additionally, NIH-funded researchers are exploring the potential of stem and progenitor cells to be reprogrammed into multiple cell types, which could be used as a source of cells to populate tissue chips. Currently, investigators are making great strides both in the reliable differentiation and maturation of induced pluripotent stem (iPS) cells into the desired cell types and in combining those cells into cellular microsystems. NIH and DARPA investigators are also beginning to integrate individual tissues (e.g., heart, lung, or nervous system) onto miniaturized platforms that combine 2-4 systems together. The goal of the project is to have a commercially viable prototype chip available at the end of the five-year award period (2017). Although a high-risk endeavor, the development of genetically diverse tissues-on-a-chip will allow assessment of personalized responses to drugs prior to clinical trials, a technological advance that will make clinical trials safer, cheaper, and more effective.

New Common Fund DARPA-like Program

The Common Fund request for FY 2015 includes $30 million for a new DARPA-like program that would utilize Other Transaction Authority (OTA) to support high risk, goal-driven activities that aim to achieve rapid technology development. One project under consideration, Bioelectronic Medicines, would seek to establish methods to stimulate the peripheral, autonomic, and enteric nervous systems and thereby control the function of physiologic systems. This could lead to proof of concept for an entirely new class of neural control devices that have the potential to precisely treat a wide variety of diseases and conditions.

Universal Influenza Vaccine

On average, more than 30,000 people in the United States die each year from seasonal influenza infections. Some of the currently circulating avian strains (H5N1 and H7N9) have also sporadically infected humans and could have pandemic potential if they were to evolve the ability for sustained human-to-human transmission. Given how rapidly influenza surface proteins evolve, new vaccines must be developed annually to protect against seasonal influenza, and as needed, to help protect against newly emerging pandemic influenza strains. Current vaccine strategies are directed to those portions of the influenza virus that change season to season. To better protect against seasonal influenza and influenza strains with pandemic potential, researchers are on the path to develop a "universal" influenza vaccine that would

induce a potent immune response to the common elements of the influenza virus that undergo very few changes from season to season, and from strain to strain. A universal influenza vaccine has the potential to protect against multiple influenza strains over several years, and potentially reduce the need for yearly vaccinations.

NIH is funding research to support the development of such a vaccine. For instance, the National Institute of Allergy and Infectious Diseases' Vaccine Research Center (VRC) is conducting studies to better understand the immune response to influenza infections and vaccine candidates, and is exploring different vaccine delivery platforms and strategies for generating broadly-neutralizing antibodies. The VRC also has supported several early-stage clinical trials of candidate universal influenza vaccines. NIAID is also funding a variety of extramural projects focused on the development of a universal influenza vaccine and on the development of immunological agents that will increase a vaccine's effectiveness when administered.

The Promise of Induced Pluripotent Stem Cells

Induced pluripotent stem cells (iPSCs) are revolutionizing the study of disease. iPSCs are derived from mature cells, typically from a patient's skin or blood, which researchers can reprogram back to an immature state. These cells can then be programmed into a wide variety of cell types, including liver cells, neurons, cardiac cells, and blood cells. Once they have been reprogrammed into different cell types, iPSCs can be used to understand the molecular pathways in biological development and human disease. The ability to manipulate these cells to answer critical scientific questions is a vital part of NIH's goal for this research investment. For example, disease-specific iPSCs have already been developed from patients with a variety of conditions, such as Alzheimer's, Long QT syndrome, Timothy Syndrome, schizophrenia, and Fragile X syndrome. These cells will be useful models for better understanding the cellular abnormalities in these disorders. NIH-supported consortia have built repositories of iPSC cells from patients with various conditions that are being used in a wide range of research.

Building on these advances in developing disease-specific stem cells, a group of NIH-funded scientists has discovered how to use human iPSCs to form groups of cells that mimic the three-dimensional organization and other specific features of the human forebrain. These 3-D cultures may provide more physiologically relevant systems to assess aberrant developmental processes relevant to a wide variety of brain disorders.

NIH is also investing in the use of iPSCs for drug development research. In Parkinson's disease research, for example, NIH-supported scientists collected skin cells from patients with genetically inherited forms of the disease and reprogrammed the cells into nerve cells that resembled those that die as a result of the disease. When the scientists tested various potential drug treatments to address the defects in the cells, they found that the cells' responses to treatments depended on the type of Parkinson's that each patient had. This use of iPSCs could help determine which patients might respond best to a particular treatment in clinical trials.

iPSCs are also being used as tools for drug screening for treatments for diseases such as amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease). ALS is an ultimately fatal disease characterized by the progressive loss of motor neurons in the spinal cord. An ideal treatment for this disease would be a drug that stabilizes human motor neurons against cell death. With NIH funding, research teams have generated iPSCs from individuals with inherited and sporadic forms of ALS and reprogrammed the cells into neurons. Researchers are now using these neurons to test potential drug candidates for their ability to reverse the ALS effects.

Another step along the pathway to human treatments with iPSCs is testing in animal models. After the first successful use of iPSCs to treat sickle cell anemia in mouse models, researchers have been working toward this goal for other diseases. In promising NIH-funded research, animal models of Duchenne muscular dystrophy showed improved muscle function after a transplant of muscle progenitor cells that were derived from iPSCs.

Moving forward, the use of iPSC technology will continue to advance the study of disease mechanisms as well as to facilitate development and optimization of treatments for patients. NIH remains committed to supporting this research through extramural research grants to institutions throughout the country and NIH intramural research programs, such as the Center for Regenerative Medicine, with the ultimate goal of using iPSCs to develop specific cells and tissues for human cell-based therapy. The clinical promise of iPSCs is generating interest worldwide, and the first clinical trial of a product developed using iPSCs—a potential therapy for age-related macular degeneration—is poised to begin soon in Japan, Additional NIH investment in this area will enable research leading to new treatments to be tested in clinical trials.

Preventing Suicide in the Military

Historically, the suicide rate among Army personnel has been lower than that for a demographically comparable civilian population. In 2004, however, the suicide rate among soldiers began rising, reaching a new record level several years in a row including 2012. This serious issue was the impetus behind the development of the Army Study to Assess Risk and Resilience in Service members (Army STARRS), the largest study of suicide and mental health among military personnel ever undertaken. A collaboration between the Department of Army, NIH's National Institute of Mental Health (NIMH), and several academic partners, this project is designed to identify, as rapidly as possible, risk and protective factors that will help the Army develop effective strategies to reduce rising suicide rates, and to address associated mental health problems among soldiers. Army STARRS's five components examine historical administrative data collected by the Army and Department of Defense as well as current data collected from soldiers in all phases of Army service. This research will help inform our understanding of suicide in the overall population, leading to more effective prevention and treatment for service members and civilians alike.

Now in its fifth year, Army STARRS is well on its way to achieving its initial goals. As of December 2013, seventy-six Army installations have been involved in the study, and more than 112,000 soldiers have volunteered to participate across all study components. All soldiers who participate are asked to complete a comprehensive survey. A subgroup of those soldiers, nearly half, also were administered a battery of neurocognitive tests. In addition, more than 43,000 soldiers voluntarily donated blood samples for biomarker analysis. The majority of study components have completed participant enrollment and have transitioned to the analysis stage. The first series of data papers were recently accepted for publication. The research team has been briefing Army senior leadership multiple times per year and is now actively engaged with the Army organizations responsible for suicide prevention in order to facilitate the translation of study findings into practical applications.

Theme 3: Big Opportunities in 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–often referred to as "Big Data"–are generated from an array of devices such as genomic sequencing machines and other high-speed technologies, novel imaging strategies, electronic health records (EHRs), and smart phone applications that monitor patient health. Sharing Big Data readily and responsibly is a critical step in translating new discoveries into clinical applications, and these efforts are consistent with wider Administration efforts to increase access to federally funded research results. However, real challenges arise when scientists try to visualize, manipulate, or mine these 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 with requisite skills to manage, analyze, store, and preserve complex scientific data is essential to realize the full value of Big Data.

Cross-cutting NIH Efforts

In 2012, NIH established an overarching initiative–termed Big Data to Knowledge (BD2K)–to accelerate the pace of discovery through the use of biomedical Big Data, to be led by the new NIH Associate Director for Data Science, Dr. Philip Bourne. By the end of this decade, the goal of BD2K is to enable a quantum leap in the ability of the biomedical research enterprise to maximize the value of the growing volume and complexity of biomedical data. To achieve this goal, BD2K will support four programmatic efforts:

- Facilitation of broad use and sharing of large, complex biomedical datasets through the development of policies, resources and standards;
- Development and dissemination of new analytical methods and software;
- Enhanced training of data scientists, computer engineers, and bioinformaticians; and
- Establishment of Centers of Excellence to develop generalizable approaches that address important problems in biomedical analytics, computational biology, and medical informatics.

Plans are already in motion to support these programs. The first funding opportunity announcement for the Big Data Centers of Excellence was released recently, and NIH has committed $24 million annually over four years to support the initial grants for this part of the BD2K program. BD2K also issued a Request for Information (RFI) for public input on developing a biomedical Data Catalogue that would enable researchers to easily find, share, and cite biomedical research data. An RFI to gather public input on the training and education needs to support the BD2K initiative was also issued. The input from the RFIs will be used to facilitate focused and actionable discussion during a number of workshops in the BD2K programmatic areas of interest. The workshops will be available to the public via webcast. In FY 2015, the total NIH investment in BD2K is estimated at $88 million, or roughly double the FY 2014 level.

In addition, through the NIH InfrastructurePlus Initiative, also established in 2012, an adaptive environment will be created at NIH that will facilitate the optimal use of Big Data in order to sustain world-class biomedical research, including enhancement of the NIH high-performance computational environment; implementation of agile and cost-effective approaches to storing and hosting highly complex and heterogeneous datasets; and continued development of an information rich environment of systems, applications, and tools. The InfrastructurePlus Initiative will be led by the NIH Chief Information Officer.

National Database for Autism Research (NDAR)

Big Data opportunities are being created to address some of our most disabling diseases and conditions. Here is just one example. Prompted by the need to accelerate progress in autism spectrum disorders (ASD) research, NIH created the National Database for Autism Research (NDAR). NDAR is a research data repository that holds genetic, phenotypic, clinical, and medical imaging data from participants in ASD-research studies. It also functions as a scientific community platform, defining the standard tools and policies to integrate the computational resources developed by scientific research institutions, private foundations, and other Federal and state agencies supporting ASD research. All data within NDAR use the same structure to

enable comparison and analysis by other qualified researchers. This secondary data analysis provides scientists with the tools to validate research results and to conduct studies using data from multiple sources to create larger sample populations.

Through strong partnerships with private organizations, such as Autism Speaks and the Simons Foundation, NDAR has incorporated data from more than 60,000 de-identified research participants into the database. Most public and private funders of ASD research have now made data sharing with NDAR an integral part of funding new research projects. At NIH, 80 percent of newly awarded human-subject grants related to ASD have an expectation for data sharing with NDAR; by 2015, virtually all NIH-funded human-subjects ASD research is expected to include these terms. This community-wide data-sharing initiative supported by NIH will make great strides in facilitating collaboration between scientists, enabling rigorous comparison of results between research studies, and preventing unnecessary duplication of experiments.

Like NDAR, multiple Big Data platforms will 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.

Combating the Challenge of Alzheimer's Disease

Alzheimer's disease (AD), the most common form of dementia, affects between 4 and 5.1 million Americans each year, slowly destroying brain regions that are critical for memory, reasoning, and even the most basic daily living skills. A recent report from NIH's Health and Retirement Study estimated the cost of caring for persons over age 70 with dementia in the U.S. was between $159 billion and $215 billion in 2010. By 2040, these costs are projected to increase dramatically to nearly a trillion dollars per year. 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. Some of the latest advances in AD research include the following:

- For the first time, a genetically engineered animal model exhibits the full array of AD-associated brain changes, further supporting the idea that increases in a molecule known as beta-amyloid causes the disease. Improved animal models are key to advancing understanding of this complex disease and testing promising interventions. For example, NIH-funded scientists are exploring an innovative technique to help repair Alzheimer's-damaged brain cells. In a mouse model of AD, they were able to trigger supporting cells of the brain, called glial cells, to regenerate into healthy, functional neurons.

In separate studies, research teams supported by NIH, including NIA intramural investigators, have reported that rare variations in the TREM2 and the PLD3 genes can double or even triple an individual's risk for developing Alzheimer's disease. TREM2 is a gene involved in inflammation and the immune response, and PLD3 appears to influence levels of toxic beta-amyloid in the brain, thought to be a main contributor to the disease process. These discoveries provide potential treatment targets for AD and important clues in understanding the disease NIH's long-term planning efforts are one component of HHS's National Plan to Address Alzheimer's Disease. As the lead agency in implementing Goal #1 of the National Plan, Prevent and Effectively Treat Alzheimer's Disease by 2025, NIH adopted milestones to guide and track the implementation of recommendations articulated in the May 2012 Alzheimer's Disease Research Summit. NIH's efforts to track research progress will be greatly facilitated by the launch of the International Alzheimer's Disease Research Portfolio (IADRP), a new, publicly available Big Data database that captures current Alzheimer's disease research investments and resources. The IADRP will enable public and private funders to coordinate research planning, leverage resources, avoid duplication, and identify promising areas of growth.

NIH continues to invest in a broad spectrum of basic discovery and translational research activities critical to the development of disease-modifying strategies to combat Alzheimer's disease, and the total funding level for FY 2015 across NIH is estimated at $566 million. In response to the President's Alzheimer's Initiative, NIH established the AD Genetics Data Warehouse–a collaborative effort between geneticists and the National Human Genome Research Institute (NHGRI) Large-Scale sequencing program to identify further genetic risk and protective factors. Now in its third phase, scientists supported by the Alzheimer's Disease Neuroimaging Initiative (ADNI) have gathered and analyzed thousands of human brain scans, genetic profiles, and biomarkers and are continually refining ways of detecting AD at the earliest stage possible. More than 35 NIH-funded clinical trials are under way, and more than 40 compounds are being tested as potential preventive and therapeutic interventions for Alzheimer's and cognitive decline. With NIH support, the U.S Department of Veterans Affairs and participating centers in 15 states are broadly implementing the Resources for Enhancing Alzheimer's Caregiver Health (REACH), the first intensive caregiver support intervention to be proven effective in ethnically diverse populations.

Theme 4: Nurturing Talent and Innovation

A diverse, well-trained, and highly creative workforce is critical to the success of biomedical research and is essential for the development of new scientific insights and the translation of these insights into improved health for all. NIH has dedicated training grants and fellowships for graduate students and postdoctoral researchers to ensure that it maintains such a workforce into the foreseeable future.

Recognizing that the behavioral and biomedical research enterprise has grown in size and complexity in the past decade, and that the NIH budget is not likely to grow significantly in the next few years, a working group of the Advisory Committee to the Director (ACD) was charged with examining the future of the biomedical research workforce in the United States.

The ACD found that although the vast majority of people holding biomedical PhDs are productively employed, the proportion of PhDs that move into tenure-track or tenured faculty positions represents a minority of the trainee outcomes. An increasing number of trainees now conduct research in non-academic venues such as government or private sector, or are in research-related areas, such as teaching or research policy.

NIH has been working to implement many of the ACD's recommendations. In FY 2013 the NIH Common Fund initiated the Strengthening the Biomedical Research Workforce Program, which aims to support innovative training approaches that will expand knowledge and skills beyond those required for academic-based scientific careers. The goal of this program is to better prepare pre-doctoral students and postdoctoral scientists for the breadth of careers in the biomedical research workforce, and to establish an awardee network to develop, share, evaluate, and disseminate best practices within the entire training community. The Common Fund issued ten Broadening Experiences in Science Training (BEST) DP7 awards to institutions across the country in September. The BEST Funding Opportunity Announcement was re-issued in FY 2014 with the aim of funding an additional group of awards. In addition, NIH announced plans to encourage the adoption of individual development plans for all trainees and report on those plans in grant progress reports (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-13-093.html).

In order to develop NIH's ability to assess the performance of its training activities, the ACD recommended that NIH improve its means of identifying and tracking more comprehensively all graduate students and postdoctoral researchers supported by NIH. Doing so will provide a sound basis for assessing workforce needs and planning future training activities. NIH's efforts to improve the tracking and analysis of training activities include automating training tables in reporting documents and establishing structured data collection programs like SciENcv (Science Experts Network *curriculum vitae*), which is a data platform that allows each researcher to record all research activity and current biographical information at a single site. SciENcv was piloted in FY 2013 (http://nexus.od.nih.gov/all/2013/11/20/test-drive-sciencv/) and its implementation will be expanded in FY 2014. These initiatives will offer comprehensive career outcomes data, will better inform prospective graduate students and postdoctoral researchers about potential careers in biomedical research, and will ease the reporting burden associated with managing training programs and reporting on career outcomes.

Increasing Diversity

Achieving diversity in the NIH-funded biomedical research workforce is critical to the full realization of our national research goals and is in the best interest of our country. Yet, despite longstanding efforts from the NIH and other entities across the biomedical and behavioral research landscape to increase the number of scientists from underrepresented groups, diversity in biomedicine still falls far short of mirroring that of the U.S. population. Further, an NIH-commissioned study revealed a disturbing shortfall in success rates for research grant (R01) applications between White applicants and Black applicants. In response to the unacceptable status quo, the NIH Director charged the ACD to provide concrete recommendations on ways to improve the recruitment and retention of individuals who are underrepresented in the NIH-funded biomedical workforce.

Delivered in June 2012,[1] the ACD's recommendations covered four general areas to encourage workforce diversity: 1) enhanced mentoring/career preparation and retention; 2) increased support for comparatively under-resourced institutions with track records for producing and supporting scientists from underrepresented groups; 3) improved research on peer review and piloting intervention testing; and 4) better data collection and evaluation. These recommendations form the backbone of NIH's Biomedical Research Workforce Diversity Initiative, a multi-pronged approach to foster and promote diversity in the biomedical research workforce.

The centerpiece of the initiative is the Common Fund's Enhancing the Diversity in the NIH-Funded Workforce Program. This Program consists of three highly integrated initiatives through which awardees will collectively develop, implement, and test novel ways of engaging, training, and mentoring young scientists and will disseminate successful approaches across the nation for large-scale impact.

The Building Infrastructure Leading to Diversity (BUILD) initiative is a set of experimental training awards designed to learn how to attract students from diverse backgrounds into the training pipeline and to encourage their persistence to become future NIH-supported researchers. BUILD is designed to provide relatively under-resourced institutions with the opportunity to develop novel approaches to training and mentoring their students, many of whom are from disadvantaged backgrounds and/or backgrounds that are nationally underrepresented in biomedical research. Through the BUILD initiative, eligible institutions will design and implement new models of research training that emphasize attainment of hallmarks of success in addition to scientific competencies and progression to further scientific training, such as ability to network effectively, creativity/innovative thinking, writing/effective communication, and leadership. The initiative will provide awards to approximately 10 institutions across the country; transformative impact will occur via nationwide dissemination of effective approaches developed through BUILD. A Funding Opportunity Announcement for BUILD awards was published in December 2013.

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

- The National Research Mentoring Network (NRMN) will create a single nation-wide network of mentors and mentees that will connect students, postdoctoral fellows, and faculty to experienced mentors; develop novel mentoring strategies; establish standards for good mentorship; provide training opportunities for mentors; and provide networking and professional opportunities for mentees (see Funding Opportunity Announcement for NRMN).
- The Coordinating and Evaluation Center (CEC) within the Diversity program will work across all components of the consortium to determine what works and for whom. CEC will coordinate activities of the consortium as a whole, work with BUILD and NRMN awardees to establish hallmarks of success at all career stages, coordinate evaluation of BUILD and NRMN activities, and disseminate successful approaches to the biomedical research and training community (see Funding Opportunity Announcement for CEC).

Beyond the Common Fund Program, the NIH will ensure that diversity is a core consideration of NIH governance by recruiting a Chief Officer for Scientific Workforce Diversity and creating an NIH Steering Committee Working Group on Diversity. These entities will:

- Conduct evaluation studies related to the review and funding of grants, to establish hallmarks of success at all career stages, to understand potential bias, and test various bias and diversity awareness training programs for NIH staff to determine the most effective approaches; and
- In collaboration with the Workforce initiative described above, 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.

Supporting Early-Career Investigators

NIH recognizes that there is a pool of talented junior scientists who have the intellect, scientific creativity, drive, and maturity to flourish independently without the need for traditional postdoctoral training. Reducing the amount of time these scientists spend in training provides them with the opportunity to start highly innovative research programs as early in their careers as possible. It also allows host institutions to invigorate their scientific communities by integrating the fresh perspectives brought by the junior investigators.

Two awards NIH uses to support early-career investigators are the NIH Director's Early Independence Award and the NIH Pathway to Independence Award. The Early Independence Award provides a way for some exceptional early-career investigators to skip postdoctoral training altogether and to begin independent research directly after completing their terminal degree, while the NIH Pathway to Independence Award is designed to facilitate a timely transition from a mentored postdoctoral research position to a stable research position with independent support at an earlier career stage than is currently the norm.

Cultivating Innovation

The past few decades have brought tremendous scientific advances that can greatly benefit medical research. While this unprecedented period of progress will hopefully continue into the foreseeable future, human health and well-being would benefit from accelerating the current pace of discovery. One way to achieve this goal is to support scientists of exceptional creativity who propose highly innovative approaches to major contemporary challenges in biomedical research. By bringing their unique perspectives and abilities to bear on key research questions, these visionary scientists may develop seminal theories or technologies that will propel fields forward and speed the translation of research into improved health.

To address this need, NIH has created three complementary programs—the NIH Director's Pioneer Award, New Innovator Award, and Transformative Research Award. Recipients of these awards are responsible for some of the most exciting new scientific breakthroughs. For example, Dr. Peng Yin and Dr. William Shih, both awardees of the New Innovator Award, created "DNA bricks," which are three-dimensional structures of synthetic DNA strands that may help develop targeted drug-delivery mechanisms. Another significant breakthrough was led by Dr. Karl Deisseroth, recipient of the Pioneer Award in 2005 and the Transformative Research Award in 2012. Dr. Deisseroth has developed a new brain-imaging technology, called CLARITY (highlighted above), that allows researchers to study a fully intact brain from both the global and microscopic perspectives.

Peer Review Innovation

Since 2007, NIH has been making substantial efforts to reduce the cost of peer review by the use of electronic meetings, non-refundable airline tickets, use of NIH conference space instead of hotels, and elimination of refreshments. That is estimated to have reduced peer review costs by $13 million per year in FY 2013 compared to FY 2007. For FY 2015, NIH will strive to achieve further savings by increasing the proportion of virtual peer review meetings to 15 percent, aiming to save an additional $2 million. As part of these efforts, NIH will monitor, assess, and report on if and how increased virtual panels broaden the reviewer community.

Conclusion

Investment in NIH is an investment in the overall health, economic strength, and global wellbeing of the country. NIH research has led to countless improvements in public health and safety, from a new treatment for cystic fibrosis to an awareness campaign that resulted in a dramatic decrease in the number of infants lost to Sudden Infant Death Syndrome to a new vaccine to prevent cervical cancer. NIH has been the economic engine driving the creation of thousands of research and development jobs. Scientists supported by NIH are at the forefront of breakthrough discoveries in all areas of biomedicine and are engaged in innovative biotechnology endeavors that will advance diagnosis and treatment for countless diseases, improving the health of all Americans while also driving the biotechnology sector. As a world leader in biomedical research, NIH is also a force for scientific diplomacy. In a world brought together through technology, NIH-funded scientists collaborate with colleagues across the globe to examine diseases that threaten health in all parts of the world. Working together to facilitate

research progress, train the next generation of biomedical researchers, and promote biosecurity, NIH strives to create a safer, healthier, more secure world.

The benefits of NIH investments are substantial, and in order for NIH to succeed in addressing the public health challenges of today and tomorrow, it must be strategic in how it deploys its resources. This requires planning and assessment of its research portfolio; as well, it must balance capitalizing on scientific opportunity and combating current public health threats, with creating the knowledge base to move quickly when new threats and opportunities appear.

In recognition of the important role that biomedical science plays in innovation and economic growth, many countries around the world have significantly increased their investment in biomedical science. Between 1999 and 2009, Asia's share (including China, India, Japan, Malaysia, Singapore, South Korea, Taiwan, and Thailand) of worldwide R&D expenditures grew from 24 percent to 32 percent, while U.S. R&D expenditures declined from 38 percent to 31 percent.[2] While the U.S. currently leads the world in R&D spending, China's increasing investment in R&D is projected to close the gap and surpass the U.S. in total R&D spending by about 2022.[3] The European Commission has also recently urged its member nations to increase their investment in research substantially, recommending budgets of €80 billion ($108 billion) in 2014–2020, a 40-percent increase over the previous seven-year period.[4] As the largest funder of biomedical research in the world, NIH must continue its efforts to train, develop, and sustain a diverse, productive workforce for continued leadership in biomedical innovation.

[2] *Leadership in Decline, United for Medical Research, 2012* http://www.unitedformedicalresearch.com/wp-content/uploads/2012/07/Leadership-in-Decline-Assessing-US-International-Competitiveness-in-Biomedical-Research.pdf

[3] *2014 Global R&D Funding Forecast, 2013* http://www.battelle.org/docs/tpp/2014_global_rd_funding_forecast.pdf?sfvrsn=4

[4] http://ec.europa.eu/programmes/horizon2020/en/what-horizon-2020

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

Programs and Measures	FY 2014 Enacted [3,4]	FY 2015 PB	FY 2015 +/- FY 2014
Research Project Grants	$16,077.332	$16,196.847	0.7%
Competing Average Cost (in thousands)	$474.181	$443.096	-6.6%
Number of Competing Awards (whole number)	8,997	9,326	3.7%
Estimated Competing RPG Success Rate (absolute rate)	17.3%	17.4%	0.1%
Research Centers	$2,713.055	$2,722.834	0.4%
Other Research	$1,824.798	$1,867.979	2.4%
Training	$752.877	$767.132	1.9%
Research & Development Contracts	$2,990.346	$3,030.746	1.4%
Intramural Research	$3,395.910	$3,435.324	1.2%
Research Management and Support	$1,528.653	$1,544.027	1.0%
Common Fund (non-add)	*$533.039*	*$583.039*	*9.4%*
Buildings & Facilities Appropriation	$128.663	$128.663	0.0%
Other Mechanisms[1]	$666.068	$668.101	0.3%
Total, Program Level[2]	**$30,150.853**	**$30,361.653**	0.7%

[1] Includes Office of the Director-Other, building repair & improvement (R&I) funds allocated for the NCI-Frederick facility, Superfund Research activities funded from the Interior appropriation, and National Library of Medicine (NLM) Program Evaluation.

[2] Includes discretionary budget authority received from Labor/HHS appropriations (ICs) and the Interior appropriation (Superfund). Also includes mandatory budget authority derived from the Special type 1 Diabetes account, and NLM Program Evaluation.

[3] FY 2014 figures are shown on a comparable basis to FY 2015, reflecting the NCBI and PA proposal.

[4] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

FY 2015 Budget Request
National Institutes of Health

Overview of Performance

The National Institutes of Health (NIH) 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 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 2015 NIH Budget Request reflects the agency's longstanding 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, 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 began reporting the amount of indirect costs paid per grant on its Research Portfolio Online Reporting Tools website (NIH RePORT) in October 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 2014-2018. In particular, NIH substantially contributes to the HHS Strategic Goal 2–Advance Scientific Knowledge and Innovation. For example, in FY 2015, in support of Objective A (Accelerate the process of scientific discovery to improve

health) under Goal 2, 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 Objective D (Increase our understanding of what works in public health and human services practice) under Goal 2, NIH will support research to identify three effective system interventions generating the implementation, sustainability, and ongoing improvement of research-tested interventions across healthcare systems.

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 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 toward 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 international entities. Joint research and training activities and other exchanges with such groups increase the leverage of NIH resources and support vibrant partnerships to help 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 process. For example, the Extramural Research Program, which includes 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 ICs. 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 NIH maintains 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[5] and five standing Working Groups[6]. 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, NIH can maximize its perspective and expertise in the development and oversight of policies common to 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 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.

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[5] *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.*

[6] *The five standing working groups are: Extramural Activities, Intramural, Information Technology, Facilities, and Management and Budget.*

Based on these reviews, leadership and their staff take appropriate actions to support research activities. For 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.

FY 2015 Budget by HHS Strategic Goal
National Institutes of Health
(Dollars in Millions)

HHS Strategic Goals	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
1.Strengthen Health Care	**$745**	**$1,003**	**$1,612**
1.A Make coverage more secure for those who have insurance and extend affordable coverage to the uninsured			
1.B Improve health care quality and patient safety			
1.C Emphasize primary & preventative care linked with community	745	1,003	1,612
1.D Reduce growth of healthcare costs while promoting high-value, effective care			
1.E Ensure access to quality, culturally competent care for vulnerable populations			
1.F Promote the adoption and meaningful use of health information technology			
2. Advance Scientific Knowledge and Innovation	**$27,021**	**$27,811**	**$26,834**
2.A Accelerate the process of scientific discovery to improve patient care	27,021	27,811	26,834
2.B Foster innovation at HHS to create shared solutions			
2.C Invest in the regulatory sciences to improve food & medical product safety			
2.D Increase our understanding of what works in public health and human service services			
3. Advance the Health, Safety and Well-Being of the American People			
3.A Promote the safety, well-being, resilience, and healthy development of children and youth			
3.B Promote economic & social well-being for individuals, families and communities			
3.C Improve the accessibility and quality of supportive services for people with disabilities and older adults			
3.D Promote prevention and wellness			
3.E Reduce the occurrence of infectious diseases			
3.F Protect Americans' health and safety during emergencies, and foster resilience in response to emergencies			
4. Increase Efficiency, Transparency and Accountability of HHS Programs	**$1,000**	**$1,011**	**$1,581**
4.A Ensure program integrity and responsible stewardship of resources	1,000	1,011	1,581
4.B Fight fraud and work to eliminate improper payments			
4.C Use HHS data to improve American health and well-being of the American people			
4.D Improve HHS environmental, energy, and economic performance to promote sustainability			
5. Strengthen the Nation's Health and Human Service Infrastructure and Workforce	**$386**	**$327**	**$335**
5.A Invest in HHS workforce to meet America's health and human service needs today & tomorrow	386	327	335
5. B Ensure that the Nation's health care workforce meets increased demands			
5.C Enhance the ability of the public health workforce to improve health at home and abroad			
5.D Strengthen the Nation's human service workforce			
5.E Improve national, state & local surveillance and epidemiology capacity			
TOTAL, Program Level	**$29,151**	**$30,151**	**$30,362**

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Budget Mechanism - Total

(Dollars in Thousands)

MECHANISM	FY 2013 Actual [2]		FY 2014 Enacted [2,3]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	25,140	$11,119,346	23,632	$10,959,764	23,236	$11,198,737	-396	$238,973
Administrative Supplements	*(1,315)*	248,370	*(1,215)*	154,272	*(1,204)*	149,179	*(-11)*	-5,093
Competing:								
Renewal	1,766	904,567	2,006	1,280,732	1,960	956,371	-46	-324,361
New	6,419	2,525,738	6,950	2,977,247	7,322	3,167,151	372	189,904
Supplements	49	8,926	41	8,231	44	8,788	3	557
Subtotal, Competing	8,234	$3,439,230	8,997	$4,266,210	9,326	$4,132,310	329	-$133,900
Subtotal, RPGs	33,374	$14,806,946	32,629	$15,380,246	32,562	$15,480,226	-67	$99,980
SBIR/STTR	1,466	638,517	1,584	697,086	1,635	716,621	51	19,535
Research Project Grants	34,840	$15,445,463	34,213	$16,077,332	34,197	$16,196,847	-16	$119,515
Research Centers:								
Specialized/Comprehensive	1,177	$1,994,721	1,128	$1,960,307	1,149	$1,962,737	21	$2,430
Clinical Research	58	370,187	58	407,107	58	402,021	0	-5,086
Biotechnology	89	156,159	88	157,710	90	170,682	2	12,972
Comparative Medicine	52	132,623	52	132,864	52	132,327	0	-537
Research Centers in Minority Institutions	21	55,055	21	55,067	21	55,067	0	0
Research Centers	1,397	$2,708,745	1,347	$2,713,055	1,370	$2,722,834	23	$9,779
Other Research:								
Research Careers	3,677	$614,651	3,715	$625,157	3,710	$626,778	-5	$1,621
Cancer Education	96	34,466	96	35,500	96	36,561	0	1,061
Cooperative Clinical Research	431	434,870	492	456,827	492	463,979	0	7,152
Biomedical Research Support	122	69,214	88	64,588	88	64,432	0	-156
Minority Biomedical Research Support	310	104,656	313	104,927	316	105,146	3	219
Other	1,748	525,628	1,778	537,799	1,804	571,083	26	33,284
Other Research	6,384	$1,783,484	6,482	$1,824,798	6,506	$1,867,979	24	$43,181
Total Research Grants	42,621	$19,937,692	42,042	$20,615,185	42,073	$20,787,660	31	$172,475
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,071	$132,034	3,126	$138,879	3,195	$141,865	69	$2,986
Institutional Awards	12,468	601,489	12,481	613,998	12,520	625,267	39	11,269
Total Research Training	15,539	$733,524	15,607	$752,877	15,715	$767,132	108	$14,255
Research & Develop. Contracts	2,339	$2,895,302	2,210	$2,990,346	2,186	$3,030,746	-24	$40,400
(SBIR/STTR) (non-add) [1]	*(120)*	*(59,137)*	*(127)*	*(64,982)*	*(127)*	*(70,995)*	*(0)*	*(6,013)*
Intramural Research	7,126	$3,282,734	7,137	$3,395,910	7,137	$3,435,324	0	$39,414
Res. Management & Support	5,580	1,485,463	5,697	1,528,653	5,697	1,544,027	0	15,374
Res. Management & Support (SBIR Admin) (non-add) [1]	*(2)*	*(3,185)*	*(10)*	*(6,084)*	*(10)*	*(5,934)*	*0*	*(-150)*
Office of the Director								
OD - Other		607,663		572,519		574,552		2,033
OD Common Fund (non-add) [1, 4]		*(513,476)*		*(533,039)*		*(583,039)*		*(50,000)*
ORIP/SEPA (non-add) [1, 4]		*(289,376)*		*(294,195)*		*(294,195)*		*(0)*
OD Appropriation (non-add) [1,4]		*(1,410,515)*		*(1,399,753)*		*(1,451,786)*		*(52,033)*
Buildings and Facilities[5]		126,013		136,341		136,663		322
Appropriation [1]		*(118,109)*		*(128,663)*		*(128,663)*		0
Type 1 Diabetes[6]		-142,350		-139,200		-150,000		-10,800
Subtotal, Labor/HHS Budget Authority		**$28,926,041**		**$29,926,104**		**$30,126,104**		**$200,000**
Interior Appropriation for Superfund Res.		74,871		77,349		77,349		0
Total, NIH Discretionary B.A.		**$29,000,912**		**$30,003,453**		**$30,203,453**		**$200,000**
Type 1 Diabetes		142,350		139,200		150,000		10,800
Total, NIH Budget Authority		**$29,143,262**		**$30,142,653**		**$30,353,453**		**$210,800**
NLM Program Evaluation		8,200		8,200		8,200		0
Total, Program Level		**$29,151,462**		**$30,150,853**		**$30,361,653**		**$210,800**

[1] All items in italics and brackets are non-add.

[2] FY 2013 and FY 2014 figures are shown on a comparable basis to FY 2015, reflecting the NCBI and PA proposal.

[3] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

[4] Number of grants and dollar amounts 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 under OD-Other.

[5] Includes B&F appropriation plus building repair and improvement (R&I) dollars appropriated to NCI for the Frederick MD facility.

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

Overall Appropriations

Department of Health and Human Services
National Institutes of Health

Overall Appropriations

FY 2015 Appropriations Language

NATIONAL CANCER INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cancer, [$4,923,238,000] *$4,930,715,000*, of which up to $8,000,000 may be used for facilities repairs and improvements at the National Cancer Institute—Frederick Federally Funded Research and Development Center in Frederick, Maryland.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cardiovascular, lung, and blood diseases, and blood and blood products, [$2,988,605,000] *$2,987,685,000*.

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to dental and craniofacial diseases, [$398,650,000] *$397,131,000*.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to diabetes and digestive and kidney disease, [$1,744,274,000] *$1,743,336,000*.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

For carrying out section 301 and title IV of the PHS Act with respect to neurological disorders and stroke, [$1,587,982,000] *$1,608,461,000*.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to allergy and infectious diseases, [$4,358,841,000] *$4,423,357,000*.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to general medical

sciences, [$2,364,147,000]*$2,368,877,000*[:*Provided*, That not less than $273,325,000 is provided for the Institutional Development Awards program].

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

For carrying out section 301 and title IV of the PHS Act with respect to child health and human development, [$1,282,595,000]*$1,283,487,000*.

NATIONAL EYE INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, [$682,077,000]*$675,168,000*.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to environmental health sciences, [$665,439,000]*$665,080,000*.

For necessary expenses [for] *of* the National Institute of Environmental Health Sciences in carrying out activities set forth in section 311(a) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (42 U.S.C.9660(a)) and section 126(g) of the Superfund Amendments and Reauthorization Act of 1986, [$77,349,000]*$77,349,000*.

NATIONAL INSTITUTE ON AGING

For carrying out section 301 and title IV of the PHS Act with respect to aging, [$1,171,038,000]*$1,170,880,000*.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to arthritis and musculoskeletal and skin diseases, [$520,053,000]*$520,189,000*.

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

For carrying out section 301 and title IV of the PHS Act with respect to deafness and other communication disorders, [$404,049,000]*$403,933,000*.

NATIONAL INSTITUTE OF NURSING RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to nursing research, [$140,517,000]*$140,452,000*.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

For carrying out section 301 and title IV of the PHS Act with respect to alcohol abuse and alcoholism, [$446,025,000]*$446,017,000*.

NATIONAL INSTITUTE ON DRUG ABUSE

For carrying out section 301 and title IV of the PHS Act with respect to drug abuse, [$1,025,435,000]*$1,023,268,000*.

NATIONAL INSTITUTE OF MENTAL HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to mental health, [$1,446,172,000]*$1,440,076,000*.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to human genome research, [$497,813,000]*$498,451,000*.

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

For carrying out section 301 and title IV of the PHS Act with respect to biomedical imaging and bioengineering research, [$329,172,000]*$328,532,000*.

NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

For carrying out section 301 and title IV of the PHS Act with respect to complementary and alternative medicine, [$124,296,000]*$124,509,000*.

NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES

For carrying out section 301 and title IV of the PHS Act with respect to minority health and health disparities research, [$268,322,000]*$267,953,000*.

JOHN E. FOGARTY INTERNATIONAL CENTER

For carrying out the activities of the John E. Fogarty International Center (described in subpart 2 of part E of title IV of the PHS Act), [$67,577,000]*$67,776,000*.

NATIONAL LIBRARY OF MEDICINE

For carrying out section 301 and title IV of the PHS Act with respect to health information communications, [$327,723,000,] *$372,851,000: Provided, That of the amounts available for improvement of information systems,* [of which]$4,000,000 shall be available [until] *through* September 30, [2015] *2016*[, for improvement of information systems]: *Provided further*, That in fiscal year [2014]*2015*, the National Library of Medicine may enter into personal services contracts for the provision of services in facilities owned, operated, or constructed under the jurisdiction of the National Institutes of Health (referred to in this title as "NIH"): *Provided further*, That in addition to amounts provided herein, $8,200,000 shall be available from amounts available under section 241 of the PHS Act to carry out the purposes of the National Information Center on Health Services Research and Health Care Technology established under section 478A of the PHS Act and related health information services.

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, [$633,267,000]*$657,471,000*: *Provided,* That up to [$9,835,000]*$29,810,000* shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network[:*Provided further*, That at least $474,746,000 is provided to the Clinical and Translational Sciences Awards program].

OFFICE OF THE DIRECTOR

For carrying out the responsibilities of the Office of the Director, NIH, [$1,400,134,000]*$1,451,786,000*, of which up to [$25,000,000] *$30,000,000* shall be used to carry out section [213] *212* of this Act: *Provided*, That funding shall be available for the purchase of not to exceed 29 passenger motor vehicles for replacement only: *Provided further*, That NIH is authorized to collect third-party payments for the cost of clinical services that are incurred in NIH research facilities and that such payments shall be credited to the NIH

Management Fund: *Provided further*, That all funds credited to the NIH Management Fund shall remain available for one fiscal year after the fiscal year in which they are deposited: *Provided further*, That $165,000,000 shall be for the National Children's Study ("NCS"), except that not later than July 15, [2014]*2015*, the Director shall estimate the amount needed for the NCS during fiscal year [2014]*2015*, and any funds in excess of the estimated need shall be transferred to and merged with the accounts for the various Institutes and Centers in proportion to their shares of total NIH appropriations made by this Act: *Provided further*, That [$533,039,000]*$583,039,000* shall be available for the Common Fund established under section 402A(c)(1) of the PHS Act: *Provided further*, That of the funds provided $10,000 shall be for official reception and representation expenses when specifically approved by the Director of the NIH: *Provided further*, That the Office of AIDS Research within the Office of the Director of the NIH may spend up to $8,000,000 to make grants for construction or renovation of facilities as provided for in section 2354(a)(5)(B) of the PHS Act*: Provided further, That the Director may direct up to 1 percent of the total made available in this or any other Act to all National Institutes of Health appropriations to activities that the Director may so designate: Provided further, That no such appropriation shall be decreased by more than 1 percent by any such transfers and that the Congress is promptly notified of the transfer*.

BUILDINGS AND FACILITIES

For the study of, construction or demolition of, renovation of, and acquisition of equipment for, facilities of or used by NIH, including the acquisition of real property, [$128,663,000] *$128,663,000*, to remain available until [September 30, 2018] *expended* [, of which up to $7,000,000 may be used for demolition].

SEC. [203] *202*. None of the *discretionary* funds appropriated in this title shall be used to pay the salary of an individual, through a grant or other extramural mechanism, at a rate in excess of Executive Level II.

SEC. [204] *203*. None of the funds appropriated in this Act may be expended pursuant to section 241 of the PHS Act, except for funds specifically provided for in this Act, or for other taps and assessments made by any office located in HHS, prior to the preparation and submission of a report by the Secretary to the Committees on Appropriations of the House of Representatives and the Senate detailing the planned uses of such funds.

SEC. [205] *204*. Notwithstanding section 241(a) of the PHS Act, such portion as the Secretary shall determine, but not more than [2.5] *3.0* percent, of any amounts appropriated for programs authorized under such Act shall be made available for the evaluation (directly, or by grants or contracts) and the implementation and effectiveness of programs funded in this title.

SEC. [206] *205*. Not to exceed 1 percent of any discretionary funds (pursuant to the Balanced Budget and Emergency Deficit Control Act of 1985) which are appropriated for the current fiscal year for HHS in this Act may be transferred between appropriations, but no such appropriation shall be increased by more than 3 percent by any such transfer: Provided, That the transfer authority granted by this section shall not be used to create any new program or to fund any project or activity for which no funds are provided in this Act: Provided further, That the Committees on Appropriations of the House of Representatives and the Senate are notified at least 15 days in advance of any transfer.

(TRANSFER OF FUNDS)

SEC. [207] *206*. The Director of the NIH, jointly with the Director of the Office of AIDS Research, may transfer up to 3 percent among institutes and centers from the total amounts identified by these two Directors as funding for research pertaining to the human immunodeficiency virus: Provided, That the Committees on Appropriations of the House of Representatives and the Senate are notified at least 15 days in advance of any transfer.

(TRANSFER OF FUNDS)

SEC. [208] *207*. Of the amounts made available in this Act for NIH, the amount for research related to the human immunodeficiency virus, as jointly determined by the Director of NIH and the Director of the Office of AIDS Research, shall be made available to the "Office of AIDS Research" account. The Director of the Office of AIDS Research shall transfer from such account amounts necessary to carry out section 2353(d)(3) of the PHS Act.

SEC. [213] *212*. (a) AUTHORITY.—Notwithstanding any other provision of law, the Director of NIH ("Director") may use funds available under section 402(b)(7) or 402(b)(12) of the PHS

Act to enter into transactions (other than contracts, cooperative agreements, or grants) to carry out research identified pursuant to such section 402(b)(7) (pertaining to the Common Fund) or research and activities described in such section 402(b)(12).

(b) PEER REVIEW.—In entering into transactions under subsection (a), the Director may utilize such peer review procedures (including consultation with appropriate scientific experts) as the Director determines to be appropriate to obtain assessments of scientific and technical merit. Such procedures shall apply to such transactions in lieu of the peer review and advisory council review procedures that would otherwise be required under sections 301(a)(3), 405(b)(1)(B), 405(b)(2), 406(a)(3)(A), 492, and 494 of the PHS Act.

SEC. [215] *214*. Not to exceed $45,000,000 of funds appropriated by this Act to the institutes and centers of the National Institutes of Health may be used for alteration, repair, or improvement of facilities, as necessary for the proper and efficient conduct of the activities authorized herein, at not to exceed $3,500,000 per project.

(TRANSFER OF FUNDS)

SEC. [216] *215*. Of the amounts made available for NIH, 1 percent of the amount made available for National Research Service Awards ("NRSA") shall be made available to the Administrator of the Health Resources and Services Administration to make NRSA awards for research in primary medical care to individuals affiliated with entities who have received grants or contracts under section 747 of the PHS Act, and 1 percent of the amount made available for NRSA shall be made available to the Director of the Agency for Healthcare Research and Quality to make NRSA awards for health service research.

National Institutes of Health
FY 2015 Congressional Justification

Language Analysis

Language Provision	Explanation
[Provided, That not less than $273,325,000 is provided for the Institutional Development Awards program.]	Recommend the language be removed because it is no longer necessary.
National Library of Medicine: "*Provided, That of the amounts available for improvement of information systems,* [of which] $4,000,000 shall be available [until] *through* September 30, [2015] *2016* [, for improvement of information systems]: *Provided further*, That in fiscal year [2014]*2015*, the National Library of Medicine may enter into personal services contracts…."	Updates year reference to ensure continuation of two-year funding availability and personal services contracts. Proposed language change clarifies that this $4 million level is meant to be a ceiling only for the purposes of the two-year funding availability.
[Provided further, That at least $474,746,000 is provided to the Clinical and Translational Sciences Awards program]	Recommend the language be removed because it is no longer necessary.
Provided further, that the Director may direct up to 1 percent of the total made available in this or any other Act to all National Institutes of Health appropriations to activities that the Director may so designate: Provided further, That no such appropriation shall be decreased by more than 1 percent by any such transfers and that the Congress is promptly notified of the transfer.	Provision provides appropriations clarity regarding the NIH Director's ability to use 1 percent transfer authority, as provided in authorizing language.
Office of the Director: "of which up to [$25,000,000] *$30,000,000* shall be used to carry out section [213] *212* of this Act…."	Updates amount for Other Transaction Authority due to new DARPA-like program proposed for the Common Fund.
Building and Facilities: "…to remain available until **[**September 30, 2018**]** *expended*...."	The Consolidated Appropriations Act, 2012 (P.L. 112-74) changed "expended" to "September 30, 2015." NIH proposes reverting back to the previous language to provide NIH maximum flexibility to administer these resources.

National Institutes of Health
FY 2015 Congressional Justification

Authorizing Legislation
(Dollars in Thousands)

National Institutes of Health:	FY 2014 Amount Authorized[1]	FY 2014 Appropriations Act	FY 2015 Amount Authorized[1]	FY 2015 President's Budget
Sec 301 and Title IV of the PHS Act	$29,926,104	$29,926,104	$30,126,104	$30,126,104
Section 330B(b)(2) of the PHS Act[2]	$150,000	$139,200[3]	$150,000	$150,000
Section 311(a) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, and Section 126(g) of the Superfund Amendments and Reauthorization Act of 1986	$77,349	$77,349	$77,349	$77,349

[1] Explicit authorization levels for NIH expired at the end of FY 2009.

[2] This represents a mandatory appropriation, for which FY 2014 was authorized and appropriated in the American Taxpayers Relief Act of 2012 (P.L. 112-240), and for which reauthorization is proposed for FY 2015.

[3] Post-sequester

NATIONAL INSTITUTES OF HEALTH

Appropriation History[1]

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2006	28,740,073,000	28,737,094,000	29,644,804,000	28,461,417,000 [2]
2007	28,578,417,000	28,479,417,000 [3]	28,779,081,000 [3]	29,030,004,000 [4]
2008	28,849,675,000	29,899,004,000	30,129,004,000	29,312,311,000 [5]
2008 Supp.				150,000,000
2009	29,457,070,000	30,607,598,000	30,404,524,000 [6]	30,545,098,000
2009 ARRA				10,400,000,000 [7]
2010	30,988,000,000	31,488,000,000	30,988,000,000	30,934,413,000 [8]
2011	32,136,209,000		31,989,000,000	30,935,000,000 [9]
2012	31,979,000,000		30,630,423,000	30,852,187,000 [10]
2013	30,852,187,000		30,810,387,000	30,929,977,000 [11]
2013 Sequestration				(1,552,593,211)
2014	31,323,187,000		31,176,187,000	30,142,653,000
2015 PB	30,353,453,000			

[1] Does not include comparability adjustments. Superfund and Type 1 diabetes are included except where indicated. Separate appropriation for Superfund Research activities at NIEHS beginning in FY 2001. Includes amounts authorized to the NIDDK for Type 1 diabetes research beginning with the FY 2002 Appropriation.

[2] Reflects: a) $2,903,664,000 appropriated to the ICs for HIV research, b) NIH share of Government-wide rescission of $287,356,000, and c) transfer of $99,000,000 to the Global Fund for HIV/AIDS, Malaria, and Tuberculosis.

[3] Reflects funding levels approved by the Appropriations Committees.

[4] Reflects: a) $2,905,802,000 appropriated to the ICs for HIV research, b) add-on for pay cost of $18,087,000, c) transfer of $99,000,000 to the Global Fund, and d) Supplemental Bill transfer of $99,000,000.

[5] Reflects: a) $2,928,345,000 appropriated to the ICs for HIV research, b) NIH share of the Government-wide rescission of $520,929,000, c) transfer of $294,759,000 to the Global Fund, and d) a supplemental appropriation of $150,000,000 reflected below.

[6] Excludes funding for Superfund Research activities for which the Appropriations Committee did not mark up a figure.

[7] Provided under P.L. 111-5.

[8] Reflects Labor/HHS appropriation of $30,705,201,000; transfer of $300,000,000 to Global AIDS funds; $1,000,000 transfer from HHS for the Interagency Autism Coordinating Committee and Secretary's 1% transfer to HHS of $4,587,000.

[9] Reflects: $3,059,277,000 appropriated to the ICs for HIV research; $998,000 transfer from HHS to the Interagency Autism Coordinating Committee.

[10] Reflects: $3,074,921,000 appropriated to the ICs for HIV research; Omnibus Across-the-Board rescission of $58,130,567 and the Secretary's transfer of $8,726,791.

[11] Reflects: Full-year continuing resolution base. Does not include Section 3004 OMB 0.2% across the board rescission.

National Institutes of Health
FY 2015 Congressional Justification

Appropriations Not Authorized by Law

This is not applicable to NIH.

Narrative by Activity

National Institutes of Health
(Dollars in Thousands)

	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 Request +/- FY 2014 Enacted
Program Level [1]	$ 29,151,462	$ 30,150,853	$ 30,361,653	$ 210,800
FTE	18,234	18,234	18,234	-

[1] Includes Mandatory Type 1 Diabetes, Superfund and NLM Program Evaluation ($8.20 million) in FY 2013, FY 2014 and FY 2015.

Authorizing Legislation: Section 301 and Title IV of the Public Health Act, as amended.

Allocation Method.....Competitive Grant
Allocation Method.....Contract
Allocation Method.....Intramural
Allocation Method.....Other

Program Description and Accomplishments

NIH continues to consider organizational initiatives and reforms to ensure that its structure is optimized. In March 2013, the Scientific Management Review Board (SMRB) voted to approve recommendations for optimizing the NIH Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. SMRB was asked to consider how NIH can support the SBIR/STTR programs in ways that encourage biomedical innovation from small businesses that align with NIH priorities, fund quality proposals yielding the greatest potential for successful commercialization, and leverage existing NIH resources and expertise to enable the success of its grantees. SMRB identified three primary areas in which the programs could be improved. First, the programs should be streamlined to reduce delays in the application, review, and award processes. Second, the programs should place greater emphasis on the selection and support of projects with a high likelihood of commercial success. Third, NIH should increase communication and collaborative efforts across the Institutes and Centers (ICs) in order to share lessons learned and leverage existing resources and expertise. In FY 2014, NIH will consider how best to implement the Board's recommendations.

In December 2013, SMRB approved findings and recommendations on approaches to assess the value of biomedical research supported by NIH. Members recommended that NIH intensify its efforts to assess systematically, comprehensively, and strategically the value of biomedical research for the purposes of accountability, effective management, and public awareness. To do this, SMRB recommended the creation of a trans-NIH committee on assessments that should oversee the selection of study topics, take further steps to standardize and link the data needed to conduct assessments, and coordinate internal and external assessment activities (e.g., grants, contracts). SMRB also advised NIH to use a mix of assessment methodologies, including representative case studies, to capture the value of biomedical research supported across NIH. In FY 2014, NIH will begin to implement these recommendations.

With respect to an earlier recommendation by the SMRB, NIH has decided not to include the Clinical Center as a line item in the annual Office of the Director budget. As a result, the Clinical Center will continue to be funded through the NIH Management Fund. This was one of several SMRB recommendations for the Clinical Center, and others have already been implemented (*e.g.,* promoting clinical research collaborations between intramural and extramural investigators, forming the Clinical Center Governing Board to provide strategic and operational oversight and make budget recommendations).

Long-Range NIH Research Contributions to Improvements in Health Care and Public Health: Selected Examples

NIH has supported biomedical research to enhance health, lengthen life, and reduce illness and disability for more than 100 years. Between 1970 and 2010, the life expectancy of the average American increased by 7.9 years.[1] Older Americans are not just living longer; they are staying healthy and active longer. Rates of reported risk factors for chronic disease (uncontrolled LDL or high blood pressure, smoking, etc.) have dropped by more than 10 percent since 1999. At age

[1] *Calculated from Health, United States, 2011: with Special Feature on Socioeconomic Status and Health, http://www.cdc.gov/nchs/data/hus/hus11.pdf*

65, Americans today can expect to live 19.2 more years – 40 percent longer than in 1950, and the vast majority of these adults continue to live without any activity limitations, a major improvement in just the past 30 years.[2] The largest growing demographic group in the United States consists of individuals living beyond the age of 85. We can attribute these remarkable improvements, in large part, to NIH research. NIH-funded projects have made many contributions that have advanced health care and enhanced public health. The following are some selected examples.

Heart Disease

Through research advances supported in large part by NIH, deaths from heart disease have fallen by more than 60 percent since 1970.[3] The identification of cardiac risk factors such as smoking, high blood pressure, and high cholesterol by the Framingham Heart Study along with NIH-supported clinical trials led to the development of effective pharmacological and behavioral interventions, as well as safe and effective surgical and catheter-based procedures to open clogged coronary arteries.

Diabetes

Adults diagnosed with diabetes during middle age used to live on average 10 years less than adults without diabetes. Thanks to the development of early screening methods and treatments that enable better control of diabetes-related complications, adults with diabetes are living longer and healthier lives. Between 1997 and 2006, the death rate among adults with diabetes declined by 23 percent for all causes of death and by an extraordinary 40 percent for cardiovascular disease.[4] These remarkable improvements are due largely to clinical trials supported by NIH. NIH research is also generating important insights into the prevention of diabetes. Studies funded through the Diabetes Prevention Program have shown that lifestyle changes, such as diet and physical activity, can lower the risk of developing type 2 diabetes by 58 percent in adults at high risk for diabetes.

Stroke

Fewer people are dying of stroke today—the age-adjusted stroke mortality rate has decreased by 70 percent since 1950 and by 33 percent since 1996. In 1995, an NIH-funded clinical trial established the first and only FDA-approved treatment for acute ischemic stroke. The drug tPA reduces the risk of disability and maximizes the potential for patient recovery. A recent analysis estimated that tPA can provide considerable cost savings—nearly $74 million annually for the first post-stroke year alone—if used in just 20 percent of all ischemic stroke patients in the US. However, tPA must be administered within three hours of the onset of symptoms; current research at NIH is working to improve public awareness of stroke and to educate high risk populations on the importance of seeking immediate medical attention.

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[2] *Calculated from Health, United States, 2010: with Special Feature on Death and Dying http://www.cdc.gov/nchs/data/hus/hus10.pdf and National Vital Statistics Reports Deaths: Preliminary Data for 2011 Vol. 61, Number 6 http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_06.pdf.*

[3] *Calculated from Health, United States, 2011: with Special Feature on Socioeconomic Status and Health, http://www.cdc.gov/nchs/data/hus/hus11.pdf*

[4] *Gregg, E.W. et al. Diabetes Care **35**, 1252–1257 (2012). CDC News: http://www.cdc.gov/diabetes/news/docs/cvd_2012.htm*

Lung Cancer

Lung cancer is the second most common cancer and is the primary cause of cancer-related death in both men and women in the United States. NIH-funded research has contributed to a decrease in mortality, lowering the death rate per 100,000 people from 59.3 in 1990 to 47.6 in 2010, a 20 percent decrease. The recent development of targeted therapies, such as erlotinib and crizotinib, has led to dramatic responses in individuals whose lung cancers harbor particular genetic mutations. Recent data from an NIH-sponsored trial indicates that low-dose helical CT scans of heavy smokers can be effective in making the diagnosis of lung cancer early enough to achieve a surgical cure.

HIV/AIDS

Each year, 50,000 people in the United States become infected with HIV, the virus that causes AIDS. Currently, there are an estimated 1.1 million people in the United States and 34 million people globally who are living with HIV infection. In 2011 alone, 1.7 million people died from AIDS-related causes. In the early 1980s when the HIV/AIDS epidemic began, people with AIDS were not likely to live longer than a few years, but now, thanks in part to research funded by NIH, there are powerful treatments that can suppress the virus to undetectable levels, allowing those infected with it to live for many years and as a result, death rates have dropped by more than 13 percent. These treatments are also now being used to prevent the transmission of HIV from mothers to children and between sex partners, providing hope that the HIV/AIDS epidemic will one day be over.

Breast Cancer

Primarily because of NIH-supported research, multiple breast cancer susceptibility genes have now been identified, including BRCA1, BRCA2, TP53, and PTEN/MMAC1. Genetic testing now allows for tailored, safer, and more efficient treatments. As a result of these and many other advances, the death rate from breast cancer per 100,000 women declined from, 33.3 to 22.1 between 1990 and 2010.

Prostate Cancer

NIH-supported research on the treatment of prostate cancer has improved surgical approaches as well as radio-, chemo-, and hormonal therapies. The success of these advances has contributed to the significant decline in the death rate. Between 1990 and 2010, prostate cancer deaths per 100,000 men dropped from 38.4 to 21.9.

Cervical Cancer

Cervical cancer is a deadly cancer in women. It is usually a slow-growing cancer that may or may not have symptoms, but it can be detected during routine gynecologic examinations. Cervical cancer is almost always caused by human papillomavirus, or HPV, infection. Due to groundbreaking NIH research, two FDA-approved vaccines (Cervarix and Gardasil) are now available to prevent infection by HPV types 16 and 18, which cause about 70 percent of cervical cancer. Efforts have been underway to scale up the use of the vaccines both in the United States and abroad.

Infant Health

In 1960, 26 of every 1,000 babies born in the United States died before their first birthday. By 2010, the infant mortality rate was 6.1 per 1,000 births, considerably less than a generation before. A sustained, long-term effort, informed in large part by NIH research, contributed to these substantial improvements in the survival rates of infants born preterm and to advances in care for all newborns.

Adolescent Risk Behavior

In the last three decades, biological, epidemiological, and social science discoveries funded by NIH have produced a detailed understanding of the risks and mechanisms that lead to drug abuse and addiction in adolescents. This knowledge in turn has informed several new science-based prevention approaches. Today, the rate of cigarette smoking by teenagers is at its lowest point since the NIH-funded Monitoring the Future (MTF) survey began tracking drug use and attitudes of teens in 1975. Alcohol use by teenagers also has steadily declined since the 1970s, but increased slightly in 2012.

Age-Related Macular Degeneration (AMD)

A major cause of blindness and the leading cause of new cases of blindness in people over age 65, age-related macular degeneration (AMD), was largely untreatable prior to the 1990s. In 1991, an NIH-funded clinical trial established the value of laser treatment for advanced AMD to stabilize the condition. In 2001, NIH researchers announced that a daily dietary regimen of antioxidant vitamins and minerals delayed the onset of advanced AMD by 25 percent. In 2012, a clinical trial supported by NIH showed that long-term treatment of AMD with either the drug Avastin or the drug Lucentis resulted in dramatic and lasting improvement in vision, such that two-thirds of patients had driving vision (20/40 vision or better). More recently, researchers are beginning to understand epigenetic changes that can occur in individuals that result in an increased risk of AMD.

Hearing Loss

NIH-supported research has driven the development of hearing aids from the first electronic hearing devices invented in the 1950s to the sophisticated digital devices available today. Innovative collaborations between NIH, the Department of Veterans Affairs (VA), and the National Aeronautics and Space Administration (NASA) have significantly improved hearing aid technology over the past 20 years. In addition to amplifying sound, today's hearing aids are able to address the challenges of understanding speech, localizing sound, and hearing in noisy environments. Furthermore, many children born with congenital deafness can now be successfully treated with cochlear implants, giving them a lifetime of hearing.

Burns and Traumatic Injury

NIH funded research on fluid resuscitation, wound cleaning, skin replacement, infection control, and nutritional support has greatly improved the chances of surviving catastrophic burns and traumatic injuries. In the mid-1970s, burns that covered even 25 percent of the body were almost always fatal. Today, people with burns covering 90 percent of their bodies can survive, although often with some impairments. From 1990 to 2010, the death rate per 100,000 people from motor

vehicle traffic injury decreased from 18.5 to 11.3, and firearm fatalities dropped from 14.6 to 10.1. These dramatic increases in survival rates, as well as increased health, functioning, and quality of life of survivors, are in large part due to research findings that have transformed clinical practice.

Science Advances from NIH Research

Thousands of new findings are reported every year by NIH-funded scientists. Many of these findings are like pieces of a complex puzzle; taken together and over time, they provide the scientific basis for significant improvements in health. Listed below are just a few of the many recent accomplishments from NIH research:

Detecting and treating autism early

A recent NIH-supported randomized clinical trial demonstrated that an intensive early behavioral intervention delivered before the age of two years can improve symptoms as well as normalize brain activity in some children with autism. This finding adds to the growing evidence that detecting and treating autism early is key to improving outcomes.

Treating autistic behaviors in a mouse

NIH intramural researchers have reversed behaviors in mice resembling two of the three core symptoms of autism spectrum disorders (ASD). An experimental compound that targets the chemical messenger glutamate, called GRN-529, increased social interactions and lessened repetitive behaviors in a strain of mice that normally display such autism-like behaviors. Similar compounds are already being tested in patients with Fragile X syndrome – the most common form of inherited intellectual and developmental disabilities – about one third of whom also meet criteria for autism spectrum disorders. These findings suggest a strategy for developing a single treatment that could target multiple diagnostic symptoms in multiple, overlapping neurological disorders.

Immune cells regulate brain development

Scientists discovered a new role for immune cells called microglia in the developing brain. Microglia serve as a primary defense against infection and tissue damage in the brain. Researchers recently found that microglia engulf healthy precursor cells in the developing, prenatal brain– a surprising finding because the best documented function of microglia is to rapidly clear away dying cells. The reason microglia feast on neural precursor cells may be to regulate brain size during development, akin to putting the brakes on the rapidly developing brain. Since past studies have linked infections and immune activation during pregnancy with neurodevelopmental disorders, this finding may reveal insights into such disorders as autism and schizophrenia.

How sleep clears the brain

NIH-funded scientists discovered a system of tiny channels in the mouse brain which appear to quickly and efficiently remove waste products. Additional research showed that the brain flushes out more built-up toxins while the animal is asleep, giving new importance to getting adequate amounts of sleep to help with everyday functions. Before this discovery, it was widely

believed that nutrients and waste were transported through the slow process of diffusion. Innovative brain imaging techniques allowed the investigators to study the intact mouse brain in real time, revealing an efficient pressure-driven system of channels located in a special type of glial cell – called astrocytes – located at the base of the blood-brain barrier. Further, malfunction of this "glymphatic system" in mouse brain slowed the clearance of amyloid beta, a brain protein that builds up in patients with Alzheimer's disease. The finding shows that the brain can cleanse itself in a more organized way and on a much larger scale than has been realized previously; it may lead to new strategies for treating neurodegenerative disorders.

NIH-funded researchers create next-generation Alzheimer's disease model

A new genetically engineered lab rat that has the full array of brain changes associated with Alzheimer's disease supports the idea that increases in a molecule called beta-amyloid in the brain causes the disease. Previously engineered animal models of Alzheimer's disease never quite represented the full-blown disease, exhibiting only modest memory problems and some, but not all, of the pathological hallmarks of the disease. The findings support a prime research objective identified during the May 2012, NIH-supported Alzheimer's Disease Research Summit 2012: Path to Treatment and Prevention, an international gathering of Alzheimer's researchers and advocates. Improved animal models are key to advancing understanding of this complex disease and testing promising interventions.

Killing cancer with radioactive bacteria

For the first time, NIH-funded researchers employed live bacteria to deliver a lethal dose of radioactivity to pancreatic cancer cells in mice without harming normal cells, offering a potential new treatment avenue against a form of cancer that is notoriously difficult to treat. An estimated 45,000+ new cases of pancreatic cancer occur each year, resulting in more than 38,000 deaths from the disease. While cancer therapy is often effective against primary tumors, pancreatic cancers are typically not diagnosed until the cancer has spread or metastasized. Using a new approach, researchers attached a short-lived radioisotope to a type of bacterium that could easily be cleared by immune responses in normal tissues but not in the heavily immune-suppressed environment of cancer cells. After injecting the radio-tagged bacteria in cancer-prone mice, the number of metastases was reduced by 90 percent compared to control mice injected with saline. With further development, this experimental approach might one day help doctors fight this deadly type of cancer in people.

Technique directs immune cells to target leukemia

Cancer Immunotherapy was designated as the 2013 Breakthrough of the Year by *Science* magazine. Using a form of targeted immunotherapy, NIH-funded clinician-scientists were able to induce remission in five adults with an aggressive form of leukemia, and who had relapsed – a situation with typically poor prognosis. Targeted immunotherapy directs the patient's own immune system to attack cancer cells. The researchers first remove immune cells known as T cells from the patient. These cells are genetically modified to produce an artificial receptor that can latch onto cancerous cells and trigger their destruction. The modified T cells are then infused back into the patient. The researchers found that all five of the patients who received the therapy were in complete remission within weeks of the T-cell infusion. The early results of this ongoing trial are extremely promising, and several more patients are now being tested.

Genomic analysis of endometrial tumors

A new study suggests that genomic classification of endometrial tumors could help guide treatment strategies. Cancer of the endometrium, the tissue that lines the uterus, is the fourth most common cancer among women in the United States. Experts predict that close to 50,000 women will be diagnosed with the disease in 2013, with more than 8,000 deaths. Investigators in The Cancer Genome Atlas (TCGA) Research Network undertook a comprehensive genomic analysis of nearly 400 endometrial tumors. Four novel genomic-based subtypes of endometrial cancer emerged from the analysis, knowledge that could help inform new diagnostic and treatment approaches. The researchers found that about 25 percent of tumors classified by pathologists as "high-grade endometrioid" have a pattern of genetic alterations much like that of serous tumors. Surprisingly, the researchers also found similarities between endometrioid and colorectal tumors. The parallels suggest that these tumors may benefit from a similar course of treatment.

Antibodies protect against range of flu viruses

Scientists have isolated antibodies that protect mice against a variety of lethal influenza B viruses. One of them also guards against influenza A viruses. The accomplishment points the way toward universal approaches to combat all influenza A and B viruses, as mentioned above. Type A viruses include the H5N1 avian virus, the 1918 pandemic flu virus and the seasonal H1N1 flu. Type A has several subtypes, but researchers recently isolated antibodies that neutralize a broad range of influenza A viruses. Influenza B viruses have received less attention than type A viruses. Type B viruses are not harbored by large numbers of animals, a requirement for creating pandemics. Nevertheless, a significant number of seasonal flu cases are caused by influenza B. To develop a universal flu vaccine or therapy, one needs to be able to provide protection against influenza A and influenza B viruses. The development of these broadly neutralizing antibodies against both virus types is a significant step toward a universal flu vaccine.

Clues in H7N9 influenza genetic sequences

Researchers quickly analyzed the novel avian influenza virus that has caused recent illness and death in China. Their effort gives clues to the virus's origin, transmissibility and treatment. Influenza virus strains are classified and named based on the viral surface proteins hemagglutinin (HA) and neuraminidase (NA). The team studied the genetic sequences of viruses isolated from four of the earliest fatal cases. The researchers found that the novel H7N9 viruses are likely to be treatable using NA inhibitors, a class of anti-influenza drugs that includes oseltamivir (Tamiflu) and zanamivir (Relenza). However, the novel strain won't likely be treatable with ion channel inhibitors, another major class of anti-influenza drugs. NIH researchers are conducting two clinical trials of an H7N9 vaccine, expected to conclude in December 2014, in order to be ready in the eventuality that the virus becomes readily transmissible between humans.

New bacteria stops malaria transfer between mosquitoes

NIH-funded scientists have found a way to infect mosquitoes with bacteria in order to break the genetic transmission of malaria, which kills approximately 660,000 people worldwide every year. Notably, the bacterial infection that would be introduced to mosquitoes is heritable and

could be passed on for as many as 34 generations of the aerial blood-suckers, rendering them immune to malaria parasites. Researchers have also demonstrated that the infection killed malaria parasites in the mosquitoes' digestive systems as well as salivary glands, the main point of transmission to humans through bites.

Implanted defibrillators boost "real world" survival

A new study linked implanted cardiac devices to improved survival rates, whether or not patients were participating in a carefully controlled clinical trial. Implantable cardioverter-defibrillators (ICDs) can save the lives of patients with heart failure. This small device is placed in the chest and monitors heartbeats and delivers electrical pulses if dangerous rhythms (arrhythmias) are detected. These pulses can normalize the heartbeat to prevent sudden cardiac arrest and death. Earlier clinical trials showed that ICDs can lengthen patient survival compared to optimal medical therapy. But it was unclear if the benefits seen in highly controlled clinical trials would hold true in real-world settings. In a recent study involving data from more than 5,000 patients, researchers found similar survival rates for real-world and clinical trial ICD participants. The researchers also found that matched ICD recipients in the real-world registry had significantly greater survival than trial participants who received only standard medical therapy.

Stiffening of the blood vessels precedes the development of hypertension

Analysis of data from the Framingham Heart Study has shown that stiffening of the blood vessels occurs before the development of hypertension (high blood pressure), a discovery that runs counter to the widely held belief that increased arterial stiffness is instead a consequence of hypertension. The finding sheds light on the mechanisms that cause hypertension and suggests new therapeutic approaches to prevent or delay its development.

Rutin shows promise as blood thinner

Researchers have shown for the first time that a substance called rutin is a promising candidate for development of a new drug to prevent blood clots. Scientists hoping to develop safer, more effective blood thinners recently identified rutin after screening nearly 5,000 molecules for their ability to block clot formation. Since it occurs naturally in many foods and is well tolerated by humans, researchers hope that it will prove useful for many patients without causing the harmful side effects that sometimes occur with currently available blood thinners.

Stabilizing vaccines and antibiotics with silk

NIH supported researchers have developed a way to use silk to store and distribute vaccines and antibiotics without having to keep them cold. By eliminating the need for refrigeration, the technique can lower costs and help expand the use of these lifesaving medical tools around the world. Currently, vaccines and antibiotics require extensive “cold chain” distribution networks to prevent the breakdown of these compounds when exposed to heat and humidity. This process is expensive and accounts for up to 80 percent of the cost of vaccines. Utilizing silk fibers to create a silk film that is inherently resistant to changes in moisture and temperature greatly enhances a vaccine’s stability. For example, the researchers found that a measles, mumps and rubella (MMR) vaccine retained more than 80 percent of its potency after storage at 45 °C (113 °F) for six months. Typically, the MMR vaccine would rapidly lose all its potency under those

conditions.

Platelet drug shows promise for treating severe, unresponsive aplastic anemia

An early-phase study at the NIH Clinical Center has shown that eltrombopag, a drug that was designed to stimulate production of platelets from the bone marrow and thereby improve blood clotting, can raise blood cell levels in some people with severe aplastic anemia who have failed to benefit from standard therapies. This encouraging study suggests that the drug can stimulate bone marrow stem cells and perhaps have wider utility than initially thought.

Lab-grown kidneys function in rats

End-stage kidney disease, or renal failure, affects nearly one million people nationwide. Renal failure can be reversed with kidney transplants from well-matched donors. But about one in five recipients has problems with organ rejection within five years, and there are not enough donated kidneys to meet demand. About 100,000 people in the U.S. are now on the waiting list for a kidney transplant. To provide new options for these patients, researchers have been exploring techniques for creating artificial kidneys and other organs. Just this year, NIH-funded scientists created artificial kidneys that can filter blood and produce urine when transplanted into rats. With further development, this approach could help the many patients who await organ transplants because their own kidneys no longer work.

Heart muscle cells derived from human embryonic stem cells may be useful in cardiac repair

Tissue engineering holds promise for regenerating damaged tissues and organs by stimulating them to heal themselves, but the approach to heart disease has been associated with worrisome complications such as arrhythmias. In a recent study, investigators transplanted heart cells grown from human embryonic cells into guinea pigs and showed that the cells electrically coupled and beat in sync with the animals' hearts. With further development, this approach may prove useful for heart attack survivors who are left with damaged heart muscle that can lead to progressive heart failure.

Stem cell research explains problems with blood cell formation in Down syndrome

People with Down syndrome—they have three copies of chromosome 21 instead of two—are born with abnormal blood counts and experience defects in blood formation throughout their lives. Researchers have now reported the successful use of induced pluripotent stem cells and embryonic stem cells to model the effects of the additional chromosome copy. They showed that when the additional chromosome is present, the formation of blood stem cells is disrupted. Not only do these results enable a better understanding of disease progression in people with Down syndrome, but the same approach can also be used to model other diseases.

Egg-producing stem cells found in women

Scientists long believed that women are born with a fixed number of young egg cells, or oocytes, which must last through their reproductive years. NIH-supported scientists were able to isolate egg-producing stem cells from the ovaries of women and observe these cells giving rise to oocytes. The finding may point the way toward improved treatments for female infertility.

Adult stem cells help regenerate injured lungs

NIH-funded researchers have reported that adult stem cells residing in the lung may enable lung structures to regenerate after catastrophic injury. A study in mice with induced lung damage found that a type of stem cell from the small airways proliferated rapidly, radiated to the injured regions, and assembled into structures resembling air sacs. These findings provide a critical new understanding that may aid in the development of cell-based therapies for chronic lung diseases that presently have no cure.

Researchers derive lung cells from embryonic stem cells

For the first time, scientists have established a procedure to direct embryonic stem cells to differentiate into lung cells—overcoming a major barrier to realizing the potential of regenerative medicine in the lung. Researchers were able to use the same differentiation strategy to produce disease-specific lung progenitor cells from induced pluripotent stem cells derived from patients with cystic fibrosis. This advance will improve scientists' ability to model lung diseases, test individual responses to treatments, and develop cell-based therapies for lung diseases.

Scientists find link between abnormal bone marrow cells and pulmonary arterial hypertension

Investigators have uncovered a new clue to the cause of pulmonary arterial hypertension, a progressive and frequently lethal disease that in many cases arises mysteriously. Findings from a recent study suggest that bone marrow-derived endothelial progenitor cells play a role in causing the vascular injury in the lung that underlies the disease.

Rare gene variants play a role in asthma susceptibility

A detailed exploration of selected DNA sequences has found rare variants of genes that influence asthma susceptibility in people of different backgrounds. Researchers determined that variants of four genes contributed to asthma susceptibility in African Americans, while a variant of one of the same genes was associated with asthma susceptibility in European Americans. The results may ultimately be useful in identifying people at risk for developing asthma.

Mobile technology approach can boost healthy eating and physical activity

A new study has suggested that a combination of mobile technology and remote coaching holds promise for encouraging healthier eating and physical activity behaviors in adults. The work focused on innovative approaches to changing multiple health behaviors.

Preclinical study shows heroin vaccine blocks relapse

NIH-funded scientists have reported successful preclinical tests of a new vaccine against heroin. The vaccine targets heroin and its psychoactive breakdown products in the bloodstream, preventing them from reaching the brain. According to the researchers, “Heroin-addicted rats deprived of the drug will normally resume using it compulsively if they regain access, but our vaccine stops this from happening.” If the vaccine works as well in human trials, it could become a standard part of therapy for heroin addiction, which is estimated to affect more than 10 million people worldwide.

Hormone may help treat diabetes

A newly discovered hormone called betatrophin prompts cells in the pancreas to multiply and produce more insulin. The finding, in mice, may lead to new ways to prevent or slow the progression of diabetes. NIH-funded researchers set out to try to identify a signal that seems to be sent by the liver to the beta cells when the insulin receptor is blocked and blood glucose levels rise. The researchers found that after the insulin receptor was blocked, one particular liver gene increased its activity significantly. They were able to show that this gene, which turned out to be one of the 20,000 genes that has not attracted much attention so far, coded for a secreted protein. Because it helps beta cells grow, they named it "betatrophin." Researchers are now looking at how this hormone may be used in humans.

Gastric bypass surgery reduces blood glucose levels and helps control type 2 diabetes

A recent study has shown that bariatric surgery can help control type 2 diabetes more effectively than medical therapy alone, and can help reduce the need for medications to lower glucose, lipids, and blood pressure. Studying patients with obesity and poorly controlled type 2 diabetes, researchers compared patient outcomes achieved through intensive medical therapy (which included lifestyle counseling, weight management programs, frequent home glucose monitoring, and the use of diabetes medications) to those obtained with intensive medical therapy in combination with bariatric surgery. After 12 months, blood glucose was reduced to levels below the diabetic range in only 12 percent of participants who received medical therapy alone, compared to upwards of 40 percent of those who also received gastric bypass. Longer studies will be needed to determine whether the metabolic improvements observed in the surgery patients will be durable and will translate to diverse racial/ethnic groups; meanwhile this finding adds to existing evidence that bariatric surgery may be a reasonable approach for treating some patients with obesity and uncontrolled type 2 diabetes.

Gut microbes affect weight after gastric bypass

Gastric bypass is a type of surgery used to treat severe obesity. In a procedure known as Roux-en-Y gastric bypass (RYGB), parts of the stomach and small intestine are removed. The procedure results in significant weight loss as well as improvements in associated conditions such as type 2 diabetes. NIH-funded researchers recently showed that the beneficial effects of RYGB surgery are due in part to changes in the gut microbial community. They collected samples of gut microbial communities from mice that had undergone gastric bypass, sham surgery, or sham surgery plus restricted diet. The samples were put into the stomachs of lean mice that were germ free and thus had no preexisting gut microbial communities. The mice that received microbes from the RYGB surgery mice lost weight and had less fat mass than mice that received microbes from either group of sham surgery mice.

Brain Patterns May Help Predict Relapse Risk for Alcoholism

Relapse to heavy drinking is a major obstacle to recovery for many alcohol dependent individuals, often triggered by stress or drinking-related cues that can induce craving for alcohol. Using brain imaging techniques, investigators found that individuals in recovery and who showed heightened activity in the prefrontal region of the brain were more likely to experience cravings for alcohol and subsequent relapse. The findings suggest that brain activity patterns

may be useful in the future to identify individuals at greatest risk for relapse, and that medications and/or behavioral interventions that target the prefrontal region of the brain may be beneficial for patients with the highest relapse risk.

Mobility for Paralyzed Patients

A promising new therapy for patients who are paralyzed after a spinal cord injury has been developed through the NIH's Rehabilitation Engineering program. Researchers developed a 16-electrode array to stimulate the membrane that surrounds the spinal cord (called epidural stimulation). The device, about the size of a french fry, is implanted in the patient's lower back near the spinal cord and sends a low-level electrical stimulation to the spinal cord, similar to a pacemaker for the heart. To date, all three of the patients who have tried the device are able to stand and voluntarily control both legs when stimulation is applied. The investigators are planning additional human and animal studies to explore the biological mechanism for recovery of voluntary movement.

3D model of opioid receptor reveals potential drug target for non-addictive pain medication

Abuse of opioids—including heroin, morphine and certain prescription painkillers—is a major public health problem. NIH researchers are seeking to develop pain medications with diminished abuse potential, which could reduce the need for highly addictive opioid medications. In a step closer to this goal, NIH-funded scientists have produced the first high-resolution, three-dimensional image of the kappa subtype of opioid receptor (KOR) – the one opioid receptor subtype known to mediate pain relief without the rewarding effects of other opiates. The 3D map reveals how the receptor binds to a molecule that occurs naturally in the brain, providing a long anticipated molecular framework for designing pain medications with less or no abuse potential.

First step-by-step snapshots of transcription initiation

When a gene is turned on—such as insulin in pancreatic cells or melanin in skin cells—an enzyme called RNA polymerase transcribes the genetic information from DNA into RNA. Errors in transcription can lead to malfunctions that may turn cells cancerous or trigger a host of other health problems. NIH-funded researchers have achieved a major advance in understanding transcription by providing the first step-by-step look at the molecular machinery that initiates the process. By re-enacting the process in a test tube and using an imaging technique called cryo-electron microscopy, they captured snapshots showing that a bevy of helper molecules bind to the DNA and assemble into a growing complex in a precise, stepwise manner. This complex provides a landing pad for the polymerase and primes the DNA for transcription. Knowing how this intricate complex forms provides a valuable framework for understanding a fundamental cellular process with important medical implications.

Proteins in the cornea yield clues to potential new class of antibiotics

The cornea, the outer protective layer of the eye, is amazingly resilient to infection. A team of NIH-supported investigators have identified small fragments of keratin proteins in the cornea that are responsible for fighting infections and pathogens. Synthetic variations of these peptides effectively killed bacteria that lead to flesh-eating disease, strep throat, staph infections, diarrhea, and cystic fibrosis-associated lung infections. These findings could lead to a powerful new class

of low-cost, non-toxic antibiotics at a time when antibiotic resistance is of growing concern.

Novel screening strategy identifies new class of antibiotics

Antibiotic resistance is a growing problem in the U.S. and around the world, and the number of new antibiotics reaching the clinic continues to decline. Recently, though, NIH-funded researchers have developed an innovative and cost-effective screening approach, called BioMAP, to identify potential new antibiotics, including some with the ability to kill drug-resistant bacteria. The BioMAP process successfully predicted known antibiotics and resulted in the identification of a new structurally unique antibiotic (named arromycin). BioMAP is a ground-breaking tool that can be used in academic as well as industrial laboratories to facilitate new natural products antibiotic discovery and address the looming antibiotic crisis.

DNA blood test for newborns may lead to early treatment for spinal muscular atrophy

Spinal muscular atrophy (SMA) is a genetic disease that attacks nerve cells, called motor neurons, in the spinal cord. SMA weakens muscles and can affect walking, crawling, breathing, swallowing, as well as head and neck control. Early treatment is critical; however, the short window of opportunity often occurs before symptoms appear. To address this challenge, researchers have developed an inexpensive and quick DNA test that could be used shortly after birth to identify newborns at risk of developing spinal muscular atrophy (SMA). The highly sensitive new test works by screening blood samples for the unique SMN1 gene mutation. If the test results are positive, a follow-up test can be done to detect an associated gene, known as SMN2, which could indicate the severity of disease. This new DNA screening test may help clinicians to diagnose SMA more quickly and start crucial treatment as early as possible.

New models improve the prediction of seasonal flu epidemics

Human influenza infections exhibit a strong seasonal cycle in temperate countries, such as the U.S. NIH-funded scientists assessed the role of humidity and other local climatic variables on influenza seasonality by modeling public health and climatic data from around the world. They concluded that there are two types of environmental conditions associated with seasonal influenza epidemics: "cold dry" conditions and "humid-rainy" conditions. The models developed through this research enable scientists and public health experts to 1) predict peak flu seasons given climate variables; and 2) identify the climate thresholds that explain different flu seasonality patterns around the world. The development of these new models enhances existing influenza transmission models and provides more accurate predictions of the timing of influenza activity worldwide.

Drug restores hearing in noise-deafened mice

Our ability to hear relies on sensory hair cells in the inner ear. When hair cells are damaged — by disease, injury, or aging — people experience hearing loss and cannot regenerate hair cells on their own. NIH-funded scientists have shown for the first time that a drug can be used to grow sensory hair cells in the inner ear of mice. The drug blocks a protein that normally prevents stem cells in the inner ear from turning into hair cells. When the drug was injected into the inner ear area containing hair cells in noise-deafened mice, the drug encouraged cells supporting and surrounding the hair cells to turn into new hair cells leading to small improvements in the mice's hearing. This is the first study to show that scientists can use a drug to partially restore hearing

in a mouse with noise-induced hearing loss.

Spontaneous gene mutations implicated in congenital heart disease

Findings from NIH's Pediatric Cardiac Genomics Consortium – an international multi-center collaborative research effort – have brought us closer to understanding the causes of congenital heart disease, the most common type of birth defect. The unprecedented large-scale genetic analysis found that spontaneous gene mutations affect a specific biological pathway that is critical to aspects of human development, including the brain and heart. An analysis using state-of-the-art sequencing and genome mapping techniques revealed that children with congenital heart disease had a greatly increased rate of spontaneous mutations among genes that are highly expressed, or active, in the developing heart. The findings will inform future research into the causes of congenital heart disease with the ultimate goals of improving treatment and eventually uncovering ways to prevent congenital heart disease in the early stages of heart formation.

Rapid test allows for earlier diagnosis of tuberculosis in children

Preliminary diagnosis of tuberculosis (TB) is currently made by examining respiratory secretions under a microscope and sending the sample to a laboratory to be cultured and identified. The results of the culture test can take more than two weeks to confirm a diagnosis. Diagnosing TB in children is further complicated because children tend to have much lower levels of the TB bacteria than adults. A new test, developed with NIH support, detects TB in children within an average of 24 hours. The availability of this rapid, accurate test in primary care settings can enable children to receive appropriate treatment quickly, decreasing the likelihood of hospitalization or other complications.

A step closer to a vaccine for malaria

A malaria vaccine being tested in an NIH-funded clinical trial was found to be safe, to generate an immune system response, and to offer protection against malaria infection in healthy adults. One of the most severe public health problems worldwide, malaria is transmitted to humans by the bite of an infected mosquito. After the bite occurs, infectious malaria parasites in the immature, sporozoite stage of their life cycle first travel to the liver, where they multiply, and then spread through the bloodstream, at which time symptoms develop. The vaccine trial found that participants who received the higher total dose of the experimental vaccine were able to generate a stronger immune response and, when exposed to mosquitoes carrying malaria, fight off infection.

Pharmacoperones and new treatments

Proteins throughout the body have specific structures that allow them to interact with each other and other molecules so that all of the body's systems can function properly. However, in many diseases, including cystic fibrosis, inherited cataracts, Parkinson's, Huntington's, and Alzheimer's, gene mutations cause proteins to misfold, changing from orderly sheets and spirals to tangled strands. While medical treatments may address the symptoms of these diseases, they cannot correct the underlying misfolded proteins. NIH-supported researchers discovered a new way for small molecules called pharmacoperones to enter cells and fix the misfolded proteins, restoring the proteins' normal functions. In mouse studies, researchers used this technique to cure a disease (also occurring in humans) that causes males to be unable to father offspring. This

new approach using pharmacoperones could affect treatment development for a wide range of diseases.

Liquid-to-gel injection aids formation of new bone

NIH-funded researchers have engineered a material that can aid the regeneration of bone tissue in irregularly-shaped craniofacial bones. The material begins as liquid at room temperature and is injected into the body at an injured site, where it turns into gel upon reaching body temperature. Once the gel is in place, researchers said, "It enables the formation of scaffolds locally and the delivery of growth factors and stem cells into defects of complex anatomical shapes with minimal surgical intervention." After bone tissue has been successfully regenerated, the gel can be changed back to liquid and released from the site.

Genetic microsurgery

A new technology called CRISPR (clustered regularly interspaced short palindromic repeats) is allowing scientists to specifically target genes for deletion, addition, activation, or suppression in what amounts to performing their own genetic microsurgery. The method harnesses a protein that is involved in a bacteria's adaptive immune response that works through precise targeting of DNA. Using this system, NIH-supported researchers have altered DNA in human cells, rats, mice, zebrafish, bacteria, fruit flies, yeast, nematodes, and crops. This wide-ranging applicability makes the technology potentially valuable for numerous applications, including treatment of genetic diseases.

Protein surface yields key ingredient for vaccine design

NIH-funded researchers used structural biology—the study of the architecture of the molecules of life—to design key parts of vaccines to protect against respiratory syncytial virus (RSV), which affects millions of infants each year, as well as HIV. When researchers found an antibody that attached tightly to the RSV's surface, they used x-ray diffraction techniques to determine the precise location of binding. They used this information to design an RSV protein to serve as an immunogen, the main component of a vaccine. Injecting this protein into animal models generated an immune response, making it a good candidate for vaccine development to prevent RSV. Similarly, another group of researchers identified important features on a surface protein of HIV and then designed a novel version of the surface protein to try to generate an immune response that would fight the infection. While more testing is warranted in both cases, this promising strategy could prove worthwhile in developing vaccines against life-threatening illnesses.

National Institutes of Health
FY 2015 Congressional Justification

Funding History [1]

2011 [2]	$30,935,000,000
2012 [3]	$30,852,187,000
2013 [4]	$29,143,262,321
2014	$30,142,653,000
2015 PB	$30,353,543,000

[1] Annual amount includes discretionary budget authority received from both Labor/HHS appropriations that fund ICs as well as the Interior, Environment & Related Agencies appropriation that supports NIH Superfund Research activities. Also includes mandatory budget authority derived from the Special type 1 Diabetes account. Excludes the PHS Evaluation Fund allocation to NLM.

[2] Includes $998,000 from HHS for General Departmental Management transfer for the Interagency Autism Coordinating Committee.

[3] Includes Secretary's transfer.

[4] Includes effect of sequestration and Secretary's transfer.

Summary of the Request: Narrative [5]

For FY 2015, the NIH requests a program level of $30.362 billion, a $211 million or 0.7 percent increase above the FY 2014 program level of $30.151 billion. Within the FY 2015 requested level, NIH will invest in areas of the most extraordinary promise for biomedical research and enhance the scientific workforce, working to recruit and retain the best and brightest from all of our nation's diverse populations to tackle major health challenges facing the Nation now and in the future. This request preserves NIH's highest priority activities. The following summary discusses estimates of budget mechanism amounts, which change throughout the course of the year due to scientific opportunities and the results of peer review. Mechanism and sub-mechanism levels are not proposed programs, projects, and activities.

Research Project Grants: Research project grants (RPGs) are the primary mechanism for funding of investigator-initiated biomedical research. These grants support new and experienced investigators in broad-based research programs. The use of RPGs as a mechanism of support covers the entire medical research continuum, from basic scientific research at the molecular and cellular levels to studies of human beings in both healthy and diseased states. Most grant applications originate with individual investigators who develop proposals for research in their area of interest. Research project grants awarded to institutions on behalf of a principal investigator support medical research activities in the areas of both the specific interests and competence of the principal investigators and in areas identified as high priority by the NIH Institutes and Centers (ICs).

NIH uses several RPG activities to support the best research applications from the most talented researchers. The most common, the traditional R01 grant, supports a single project with a principal investigator or co-investigators. Another frequently used grant is the P01, a multi-project grant, which supports a variety of broad-based multi-disciplinary projects conducted by numerous investigators working on various aspects of a specific major research objective or theme.

Budget Policy:
The FY 2015 President's Budget estimate for this high priority mechanism is $16.197 billion, or a 0.7 percent increase over the FY 2014 Enacted level. This level of support enables NIH to nominally increase the pace and scope of ongoing research, as well as stimulate participation of new researchers and the accompanying development of fresh ideas. To maximize the number of new and competing grants, in FY 2012 inflationary increases for future year commitments were discontinued for all competing and non-competing awards, however adjustments for special needs (such as equipment and added personnel) will continue to be accommodated. The average cost of new and competing RPGs is estimated to decrease by 6.6 percent compared to FY 2014. This is due to a cohort of very large grants that are expected to be awarded in FY 2014 and will become non-competing in FY 2015. The request is estimated to fund a total of 34,197 RPGs, essentially to the same as the number of grants anticipated in FY 2014. Of total funding, $4.132 billion would support an estimated 9,326 new and competing RPGs, an increase of 329 over the

[5] *All referenced amounts reflect adjustments for comparability to FY 2015 for the proposed direct funding of the National Center for Biotechnology Information / Public Access in the National Library of Medicine.*

8,997 new and competing RPGs estimated for FY 2014. The amount allocated for these grants would decrease by $133.9 million, or about 3.1 percent, while the amount allocated for non-competing RPGs would increase by $239.0 million, or about 2.2 percent. Administrative Supplements would receive approximately $149.2 million in FY 2015, a decrease of $5.1 million compared to the $154.3 budgeted for FY 2014. NIH will also enhance its strong commitment to extramural grants targeted to small business innovative and technology transfer research (SBIR/STTR) programs. SBIR/STTR grants would receive $716.6 million to support an estimated 1,635 awards, a $19.5 million increase, or 2.8 percent, compared to the $697.1 supported in FY 2014 – meeting the increased minimum set-aside thresholds for FY 2015 established under the SBIR/STTR Reauthorization Act of 2011.

Research Centers: Research center grants are awarded to institutions on behalf of a program director and a group of collaborating investigators to: (a) provide long-term support for leading-edge research; (b) conduct multi-disciplinary programs of biomedical research; and (c) develop research resources. The Research Centers program aims to integrate basic research with applied research and transfer activities; to promote research in the areas of clinical applications with an emphasis on intervention, including prototype development and refinement of products, techniques, processes, methods, and practices; to develop and maintain the biotechnology and research model resources needed by NIH-supported biomedical investigators for conducting research; and, to assist minority institutions in improving their research infrastructure.

Budget Policy:
NIH estimates a slight increase of support for Research Centers in FY 2015; at $2.723 billion this represents a $9.8 million increase, or 0.4 percent, compared to the FY 2014 Enacted level. This level would fund an estimated 1,370 awards, or 23 more grants than the 1,347 projected for FY 2014.

Other Research: NIH continues to support a variety of investigator-initiated activities through other types of research grants. Through the Research Careers program, NIH provides increased career opportunities in medical research to scientists of superior potential. The program provides support for young investigators who desire advanced development and scientists who need experience to qualify for senior positions. Other Research mechanisms include support for research initiatives in the cooperative clinical research sub-mechanism to encourage regionally-based clinical evaluations of methods of therapy and prevention strategies. Minority Biomedical Research Support Grants fund research that enriches the biomedical research environment at undergraduate institutions. Moreover, these grants strengthen the research training capabilities of minority faculty and students. Other Research grants also support grants for: shared resources for grantee institutions; purchase of equipment; implementation of the Nanotechnology program of the Common Fund; and conference grants to support investigator-initiated meetings, conferences or workshops to promote sharing of scientific knowledge and address specific issues.

Budget Policy:
The $1.868 billion estimated for this mechanism reflects an increase of $43.2 million, or 2.4 percent, relative to the FY 2014 Enacted level. That amount would fund a total of 6,506 grants, an increase of 24 awards or 0.4 percent over the FY 2014 level.

Research Training: The purpose of the Ruth L. Kirschstein National Research Service Awards (NRSA) program is to strengthen the Nation's corps of biomedical and behavioral research investigators. Through institutional awards and individual fellowships, NIH supports both basic and applied research training in the biomedical and behavioral sciences. Institutional awards provide the foundation for the manpower development effort by supporting the national capacity for excellent, up-to-date training in a variety of institutional settings. They enable NIH to aid institutions in maintaining vigorous and effective research training programs and, in particular, to support research training programs in areas of national need. Funds are awarded for predoctoral and postdoctoral stipends and for tuition where warranted, with a modest allocation to the institution to defray training-related expenses not covered by tuition. NRSAs also include funds for travel, fees, indirect costs, and other expenses. Stipend levels constitute the largest portion of NRSA funding.

Budget Policy:
NIH proposes an average stipend increase of 2.0 percent above the FY 2014 level for trainees. This increase is consistent with stipend modifications recommended previously by the Advisory Committee to the NIH Director. More robust stipends were also embodied in recommendations included in a major training research study issued in 2011 by the National Research Council of the National Academy of Sciences.[6] In addition, this increase is consistent with 42 USC 288(b)(5), which anticipates periodic adjustments in stipends "to reflect increases in the cost of living." Stipend rate adjustments continue a long-term strategy that NIH has used to more closely align stipend levels to salaries that could be earned in related occupations. The proposed stipend increase is intended to improve NIH's ability to attract high-quality research investigators to the field of biomedical research. In order to achieve NIH's research objectives, it is essential to ensure that highly trained scientists will be available to address the Nation's biomedical, behavioral and clinical research needs. NIH estimates $767 million for this mechanism in FY 2015, a $14 million, or 1.9 percent, increase above the FY 2014 Enacted level. That amount would support an estimated 15,715 total Full-Time Training Positions (FTTPs), 108 more than the 15,607 total FTTP funded by the FY 2014 Enacted level.

Research and Development (R&D) Contracts: NIH awards R&D contracts to acquire specific products, services or studies from academic institutions and nonprofit and commercial organizations. This mechanism also includes collaborative research efforts with other agencies, small business innovation research and architect-engineering services contracts.

Budget Policy:
FY 2015 funding for R&D contracts would increase by $40.4 million to $3.031 billion, an increase of approximately 1.4 percent above the FY 2014 Enacted level of $2.990 billion. The estimated amount would fund 2,186 contract awards, essentially the same as the number of awards anticipated in FY 2014.

Intramural Research: Through the Intramural Research Program (IRP), NIH conducts basic

[6] *National Research Council, Research Training in the Biomedical, Behavioral, and Clinical Research Sciences, (Washington, DC, The National Academies Press, 2011)*
(http://grants.nih.gov/training/Research_Training_Biomedical.pdf)

and clinical research at its on-campus research facilities in Bethesda, Maryland, and at off-campus locations such as the Gerontology Research Center in Baltimore, Maryland; Research Triangle Park, North Carolina; the Rocky Mountain Laboratories in Hamilton, Montana and Phoenix, Arizona. Fundamental research performed by intramural scientists provides the basis upon which advances in medical and dental care are built. An important byproduct of this research productivity is the cadre of young physicians and basic scientists who are trained in the techniques and approaches of intramural scientists. Many of these young researchers become extramural and intramural investigators. A valuable and unique feature of the NIH IRP is the Clinical Research Center, a 240-bed research hospital on the NIH campus. This world-class national resource promotes translational research -- that is, the transference of scientific laboratory research into applications that benefit patient health and medical care. The "bench-to-bedside" approach adopted in 1953 locates patient care units in close proximity to cutting-edge laboratories conducting related research, which facilitates interaction and collaboration among clinicians and researchers. Most importantly, patients and their families at the Clinical Center benefit from the signature elements of NIH (i.e. cutting-edge technologies, research programs, and compassionate care).

The IRP supports vital research being conducted at NIH by some of this Nation's top scientists. This powerful network of investigators is an integral part of the greater national research network devoted to advancing the knowledge needed to develop treatments, tests, and prevention strategies to benefit the public as quickly as possible. A strong intramural program at NIH complements and reinforces the work being carried out in the extramural biomedical research community.

Budget Policy:
This mechanism is estimated at $3.435 billion, a $39.4 million, or 1.2 percent, increase above the FY 2014 Enacted level. This level covers a projected 1.0 percent increase for full-time equivalent (FTE) payroll attributable to annualization of the January 2014 pay raise of 1.0 percent and the proposed January 2015 pay raise of 1.0 percent for civilian employees. Higher benefit costs linked to OPM mandated increases in the FERS agency contribution rate beginning in FY 2015 as well as projected growth in health insurance premium payments are also accommodated.

Research Management and Support (RMS): This mechanism supports many functions, including: scientific direction and management by NIH staff in the review, award, and performance monitoring of extramural awards (research grants, training awards, and research and development contracts); administrative and technical support for Congressionally-mandated review groups and advisory councils; liaison among NIH and Departmental components, as well as among applicants, grantees, advisory bodies, and special interest organizations; and monitoring of advances emerging from basic science laboratories to determine possible clinical applications for treatment and prevention. Management and administrative functions for each IC are also supported by this mechanism. Examples of such functions include: interpreting, analyzing, and implementing new legislation and administrative orders; formulating and executing IC budgets; performing management evaluation studies; determining manpower requirements; assessing the condition of both NIH and extramural grantee laboratory facilities and equipment; supporting prevention and education activities, including development of educational and informational materials for both the medical community and the general public;

and providing the leadership and business functions for the ICs.

Budget Policy:
RMS is estimated at $1.544 billion, an increase of $15.4 million or 1.0 percent above the FY 2014 Enacted level. This level covers a projected 1.0 percent increase for full-time equivalent (FTE) payroll attributable to annualization of the January 2014 pay raise of 1.0 percent and the proposed January 2015 pay raise of 1.0 percent for civilian employees. Higher benefit costs linked to OPM mandated increases in the FERS agency contribution rate beginning in FY 2015 as well as projected growth in health insurance premium payments are also accommodated.

Office of the Director: The Office of the Director (OD) provides leadership, coordination, and guidance in the formulation of policy and procedures related to biomedical research and research training programs. To provide this direction, the OD centrally coordinates NIH's extramural and intramural research activities; science policy and related social, ethical, and legal issues; technology transfer and intellectual property protection policies; health information dissemination and public education functions; legislative activities; and, oversight of the agency's stewardship of public funds.

OD encourages and fosters cross-Institute NIH research and research training efforts in the prevention and treatment of disease through program coordination offices that complement the efforts of the ICs. These offices focus on Acquired Immune Deficiency Syndrome (AIDS); women's health; disease prevention; science education; dietary supplements; rare diseases and disorders; and behavioral and social sciences research. While OD provides the overall direction, coordination and oversight of these programs, the ICs manage the actual research operations.

The OD request also includes the NIH Common Fund that supports cross-cutting, trans-NIH programs that require participation by at least two NIH ICs. The requirements for the Common Fund encourage collaboration across the ICs, while providing NIH with flexibility to determine priorities for Common Fund support.

Budget Policy:
The FY 2015 request of $1.452 billion reflects an increase of $52.0 million, or 3.7 percent, compared to the FY 2014 Enacted level. The Office of Research Infrastructure Programs and the Science Education Partnership Program would receive $294.2 million – the same level as planned for FY 2014. The OD Common Fund would receive $50.0 million above the FY 2014 level, a 9.4 percent increase that includes $30.0 million for a new DARPA-like program to achieve rapid technology development. A total of $165.0 million would be provided for the National Children's Study, which is the same amount appropriated for FY 2014.

Buildings and Facilities: The buildings and facilities (B&F) program is responsible for the design, construction, improvement, and major repair of clinical and laboratory buildings and supporting facilities essential to NIH's research mission. This account has two major elements: the design and construction of new facilities for NIH research programs and the continuing repair and improvement of existing facilities.

Budget Policy:

This request would provide $128.7 million for B&F, the same as the FY 2014 Enacted level. In addition to this is the $8.0 million budgeted in the National Cancer Institute for facilities repairs and improvements (R&I) at the National Cancer Institute—Frederick Federally Funded Research and Development Center in Frederick, Maryland. The amount identified in FY 2015 for R&I projects at the NCI Frederick facility is the same as the FY 2014 level. The requested amount for B&F projects allows NIH to continue to support the Administration's commitment to reducing water use and greenhouse gas emissions, improving building energy efficiency, and substituting renewable resources for fossil fuels in transportation assets.

Explanation - Other Activities

Type 1 Diabetes: A special program for research on Type 1 Diabetes was established by law in 1998 and is supported through a mandatory appropriation.

Budget Policy:
This program's current authorization expires at the end of FY 2014 and reauthorization is proposed at $150 million a year for three years. The FY 2015 request of $150 million for these activities represents an increase of $10.8 million, or 7.8 percent, compared to the FY 2014 post-sequester level of $139.2 million.

Superfund: NIH's contribution to the Superfund Program is to improve human health by addressing and preventing diseases and injuries associated with environmental contaminants. The Superfund Research Program (SRP) and the Worker Training Program (WTP) complement each other to create effective community and workplace public health interventions aimed at preventing harmful exposures.

Budget Policy: The FY 2015 request of $77.4 million is the same as the FY 2014 Enacted level.

NCBI/Public Access: The FY 2013 and FY 2014 levels in the request reflect comparable adjustments in the Institutes and Centers to centralize support for the National Center for Biotechnology Information and public access in the National Library of Medicine (NLM) (see pp. ST-3 and ST-4). NLM has operated these programs with additional support from the Institutes and Centers, and NIH leadership believes that consolidating funding and providing it directly to NLM will allow for more effective oversight and management of these important programs.

Opportunity, Growth, and Security Initiative

Three months ago, through the Bipartisan Budget Act of 2013 (BBA), Congress came together on a bipartisan basis and took an important first step toward replacing the damaging cuts caused by sequestration with longer-term reforms. Recognizing the importance of the two-year budget agreement Congress reached in December, the President's Budget adheres to the BBA's discretionary funding levels for FY 2015, giving Congress a roadmap for how to write a budget at those levels that promotes growth and opportunity, enhances national security, and makes important reforms.

However, the BBA levels are not sufficient to expand opportunity to all Americans or to drive the growth our economy needs. The BBA replaced half the sequestration cut for FY 2014 but just one-fifth of the scheduled cut in the discretionary funding level for FY 2015. As a result, taking into account unavoidable growth in programs such as veterans' medical care and other factors, the BBA non-defense discretionary funding levels for FY 2015 are below the levels Congress provided in the bipartisan Consolidated Appropriations Act of 2014. They are also below the FY 2007 funding levels adjusted for inflation, even though the need for pro-growth investments in infrastructure, education, and innovation has only increased due to the Great Recession and its aftermath.

For that reason, the Budget also includes a separate, fully paid for $56 billion Opportunity, Growth, and Security Initiative. This Initiative, which will be split evenly between defense and non-defense funding, shows how additional discretionary investments in FY 2015 can spur economic progress, promote opportunity, and strengthen national security. Moreover, the Opportunity, Growth, and Security Initiative is fully paid for with a balanced package of spending cuts and tax loophole closers, showing that additional pro-growth investments are easily affordable without increasing the deficit if Congress will enact common-sense spending and tax reforms.

At NIH, the Opportunity, Growth, and Security Initiative will support additional biomedical research investments that will increase understanding of underlying disease causes and spur development of innovative diagnostics, treatments, and preventive approaches to improve health, by providing an additional $970 million to restore NIH to the level proposed in the FY 2014 President's Budget. The amounts shown would be in addition to the level for these activities proposed within the base Budget request (*e.g.,* while the base Budget request for the BRAIN Initiative is $100 million, enactment of the Opportunity, Growth, and Security Initiative would bring that level to $200 million). This list is not exhaustive and additional resources would be allocated strategically to support emerging research opportunities and other signature projects.

New and Competing Research Project Grants (RPGs) ($280 million): This would provide funding for approximately 650 additional new and competing RPGs in FY 2015, for an estimated total of 9,976 awards when combined with the base Budget request estimate of 9,326 awards.

Alzheimer's Disease ($100 million): Alzheimer's disease already afflicts five million Americans and costs the Nation approximately $200 billion per year in health costs – and those numbers are predicted to rise steadily as the population ages. Recent advances in our understanding of the genetics and biology of the disease have identified new potential targets for innovative therapies to slow and ultimately prevent this devastating disease. Ramping up research, extending from basic studies of disease mechanism to clinical trials, is our best hope for turning around an increasingly serious public health problem.

BRAIN Initiative ($100 million): The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative was announced by the President in April 2013. At NIH, an extraordinary team of neuroscientists has developed an exciting new plan to unlock the secrets of brain function by defining the flow of information, or circuitry, among brain cells. Drawing on cutting edge technologies, this initiative is poised to revolutionize the diagnosis, prevention, and treatment of brain disorders. The first year (FY 2014) of funding for BRAIN at NIH is $40

million, and a steep ramp-up in FY 2015 will to allow this project to capture the momentum needed for ultimate success.

Big Data to Knowledge (BD2K) ($90 million): Technological advances have fueled the generation of increasingly larger and more complex biomedical data sets. NIH's BD2K program will facilitate sharing of data among researchers across the nation, develop faster and more accurate analytical methods, and establish Centers of Excellence to help solve the most intractable Big Data problems to deepen our understanding of disease and speed translation of new treatments.

Accelerating Medicines Partnership (AMP) ($50 million): Just announced on February 4, 2014, NIH has formed an unprecedented partnership with ten pharmaceutical companies to speed efforts identify new therapeutic drug targets, initially focusing on three disease areas in urgent need of better treatments: Alzheimer's disease, type 2 diabetes, and the autoimmune disorders lupus and rheumatoid arthritis. In FY 2015 there is an opportunity to expand AMP to two more diseases: schizophrenia would be one, and the other would be decided after industry consultation. These projects will serve as the foundation for an entirely new approach to the development of the next generation of drugs.

Vaccine Development ($125 million): Recent advances in structural biology and immunology open an entirely new window to effective vaccine development for both HIV/AIDS and influenza. In both instances, key components of the virus have been identified that do not vary from year to year or strain to strain. This defines a multiyear pathway to an effective HIV vaccine and to a universal influenza vaccine that could greatly reduce the potentially catastrophic outcome of the next influenza pandemic, and potentially reduce the need for yearly injections for seasonal flu.

Evidence and Innovation Strategies

The American public has entrusted the NIH with the Nation's largest investment in biomedical research. As a steward of public funds, the NIH is responsible for using its resources effectively to address the many health challenges that face our nation and the world. The NIH uses a well-established, rigorous decision-making process that relies on scientific expertise and stakeholder input when reviewing proposed projects and setting research priorities, while it continually seeks to improve its ability to assess the value of the research it supports. By enhancing the understanding of the results of its activities, the NIH can continue to make informed decisions for future investments and further increase the value it provides to society.

Systematically and comprehensively capturing improvements in public health that can be clearly linked to the public's investment in the NIH-funded research remains a challenge. By its nature, research is a long-term endeavor. Research outcomes cannot be foreseen with certainty, and unplanned results are common, which often provide new information that increases our understanding and may lead to redirecting the course of research activities. In some cases, the downstream impact or application of research findings is not known without further development by other entities. Despite the inherent challenges in evaluating biomedical research programs, the NIH has long engaged in activities to build a strong evidence base for current and future programs.

The NIH uses portfolio analysis tools to enhance analytic capabilities to extract meaningful information about fields of science, characteristics of research portfolios, and the outputs of research funding. Such analyses can inform the NIH about research needs and opportunities and priority setting both within and across the organization. The agency is actively identifying and developing new tools that expand and advance NIH-wide efforts in portfolio analysis; applying and disseminating current and newly developed tools to analyze biomedical research funding and the resulting impact; and promoting trans-NIH coordination of portfolio analysis activities and enhancing collaboration and training on these efforts. Portfolio analysis efforts have already proven useful in decision-making. For example, all concepts that are selected for potential funding by the Common Fund undergo portfolio analysis to understand the current state of the science in each field and identify the research goals and unique opportunities where a Common Fund investment can have the greatest impact.

The NIH also relies on program evaluation to generate a broad range of information about program performance and its context to support decision-making. Depending on its focus, an evaluation may examine the operations and outputs of a program, the extent to which program goals have been achieved, the factors that have impeded or contributed to its success, or how it may be modified to be more efficient and effective. Evaluation results are used to develop recommendations to provide appropriate level of support to a program, restructure program components, modify program goals, and/or support other program activities. The NIH frequently engages outside experts, such as the National Academy of Sciences, to conduct objective evaluations and provide independent, credible reports that offer advice and strategies to inform future research studies and investments.

To better support a wide range of analytic and evaluation activities, the NIH is working to strengthen its data and information technology infrastructure. In 2013, the Research Portfolio Online Reporting Tools (RePORT) program and several other NIH program analysis and reporting infrastructure initiatives were organized into a single entity for a coordinated NIH-wide effort. The NIH has begun to build an infrastructure that integrates the agency's administrative data on research programs with other sources of information to support evidence-based decision-making, including the long-term results of NIH-funded research found in research publications and patents. Some of this information has already been made publicly available in the RePORT Expenditures and Results database at http://projectreporter.nih.gov. Efforts are currently underway to increase the data integration and informatics capabilities needed to support assessment projects.

In addition, the new Research Performance Progress Report (RPPR) was recently implemented at the NIH. The RPPR will be used by all Federal agencies that award research and development grants, and will collect data on scientific products such as publications, patents, databases, software, new animal models, curricula, protocols, clinical interventions, and other data that result from the NIH's research funding. This effort to develop a standard method for documenting research products across the NIH and across the Federal government not only reduces the burden for grantees, but also provides a better foundation for making linkages across datasets, and has the potential to produce outcomes reporting that enables cross-agency comparisons.

Both the generation of knowledge and the application of that knowledge to health, as well as the impacts of these pursuits on the broader society, are vital parts of the NIH's value. A better understanding of all aspects of the NIH's work will lead to increased efficiency and effectiveness of that work. In 2013, the NIH Director charged the Scientific Management Review Board (SMRB), one of the agency's advisory groups, with identifying the best methods and strategies for assessing the value of NIH-supported research. NIH is working to identify strategies to implement the SMRB recommendations that willuse a more comprehensive, systematic, and strategic approach to build the evidence base for biomedical research.

Key Outputs and Outcomes Table
(NIH)

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
SRO-2.1 By 2015, evaluate islet transplantation in combination with immune modulation strategies for the treatment of type 1 diabetes in clinical trials. (Outcome)	FY 2013: Enrollment in CIT-07 was completed in FY 13, and enrollment in CIT-06 is near completion. Target: Complete enrollment in CIT-07 (Phase III trial); continue to enroll in CIT-06 (Phase III trial). (Target Met)	Perform the primary endpoint analysis in CIT-07, which is a clinical trial of islet transplantation (alone) in Type 1 diabetes.	Evaluate islet transplantation in combination with immune modulation strategies for the treatment of type 1 diabetes in clinical trials.	N/A
SRO-2.8 By 2013, advance two emerging new strategies for treating muscular dystrophy to the point of preparedness for clinical trials. (Outcome)	FY 2013: The small molecule biglycan as well as antisense oligonucleotides are two therapies that have successfully treated symptoms of muscular dystrophy in animal models. Target: Test two new strategies for treating muscular dystrophy in preclinical models. (Target Met)	N/A	N/A	N/A
SRO-2.9 By 2015, advance understanding of social determinants of health and health disparities using multilevel, trans-disciplinary team science approaches by developing intervention models of how various factors affect individual health outcomes and their distribution in populations. (Outcome)	FY 2013: Teams of trans-disciplinary scientists at NIH Centers for Population Health and Health Disparities have developed multilevel intervention strategies directed at more than just individual behavior change to prevent disease burden and improve public health. Target: Develop interventions directed at more than two factors (such as both individual level and social context) and more than just individual behavior change. (Target Met)	Test interventions at various levels to establish optimal strategies for reducing health disparities/inequities.	Implement intervention models for reducing health disparities/ inequities in various populations and identify commonalities for interventions in various underserved populations.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
SRO-2.10 By 2014 identify three clinical candidate compounds for rare or neglected diseases. (Outcome)	FY 2014: Preclinical safety and efficacy testing has been completed for all four active pilot projects and early stage clinical testing has been initiated on the four lead compound series. Target: Conclude preclinical safety and efficacy tests and initiate early stage clinical testing in conjunction with regulatory efforts on the selected rare and neglected disease lead compound series (Target Exceeded) Measure achieved earlier than anticipated.	Conclude preclinical safety and efficacy tests and initiate early stage clinical testing in conjunction with regulatory efforts on the selected rare and neglected disease lead compound series	N/A	N/A
SRO-2.11 By 2016, conduct studies of young children to determine whether the plant estrogens in soy formula produce hormone-like effects. (Outcome)	FY 2013: 1,255 Infant Phase visits were completed. Target: Complete 100 Infant Phase study visits. (Target Exceeded)	Complete 180 Infant Phase study visits	Finalize 8 datasets (including ultrasound, anthropometry and physical exam data) and begin analyses of these datasets.	N/A
SRO-3.1 By 2013, identify at least one clinical intervention that will delay the progression, delay the onset, or prevent Alzheimer's disease (AD). (Outcome)	FY 2013: Treatment phase of the IVIG study was completed and results were analyzed and presented. Target: Complete treatment phase for the IVIg study and analyze data. (Target Met)	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
SRO-3.4 By 2015, evaluate an HIV vaccine candidate in a test of concept (phase IIB) efficacy trial in order to move towards an HIV/AIDS vaccine. (Outcome)	FY 2013: Researchers tested DNA/MVA vaccine in non-human primates and phase 1trials; showing the induction of durable CD4 and CD8 T-cell and binding antibody responses. Target: Advance at least one promising candidate vaccine so that it is ready to move forward into a phase II trial. Previous target: Advance at least one promising candidate vaccine into a phase II trial. (Target Met)	Initiate the early phase testing needed to advance a promising candidate vaccine into efficacy testing.	Initiate a suite of studies to support efficacy evaluation and licensure of an HIV vaccine.	N/A
SRO-3.5 By 2013, identify and characterize at least 2 human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies. (Outcome)	FY 2013: NIH researchers identified genomic variants that were associated with risk for alcohol dependence. Target: Complete genome wide association and functional studies and identify potential genomic variants associated with risk for substance use and/or psychiatric disorders. (Target Met)	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
SRO-3.7 By 2013, develop at least two novel therapies for immune-mediated disease. (Outcome)	FY 2013: Conducted follow-up and conducted laboratory studies to explore in greater detail pre- and post-therapy samples. Target: Conduct long-term follow-up of patients in the study of rabbit and horse ATG in the treatment of severe aplastic anemia, and conduct laboratory experiments to explore in greater detail pre- and post-therapy samples. (Target Met)	Begin patient enrollment in a clinical trial for Behcet's disease.	Design a follow-up study that refines therapeutic dosages of anakinra or targets a second pathway using IL-1β monoclonal antibodies in Behcet's disease.	N/A
SRO-3.8 By 2017, determine the optimal tailored treatment regimen for patients with early stage breast cancer that maximizes the benefits of chemotherapy while minimizing the side-effects of unnecessary treatment. (Outcome)	FY 2013: Due to major changes in the cooperative group trials network in FY 13, the first in 50 years, only 50% of the hormone receptors were done in 2013 as opposed to 60%. The results from the ER testing will not be released until the definitive trial results have been obtained; this delay will not impact the timing of the reporting of the results. Target: Complete hormone receptor scoring for 60% of all cases. (Target Not Met)	Complete hormone receptor scoring for 90% of all cases.	Complete hormone receptor scoring for 100% of cases.	N/A
SRO-3.9 By 2020, identify two molecular-targeted therapies for disorders of the immune system in children. (Outcome)	FY 2013: Researchers have identified a genetic variant that confers an increased risk of developing systemic juvenile idiopathic arthritis (sJIA) and that indicates the CD4+ T cell activation pathway as a therapeutic target. Target: Identify at least one	Design a clinical trial testing an agent for a disorder of the immune system in children (e.g., Still's disease).	Complete a clinical pilot study in patients with a pediatric cohort of patients with a disorder of the immune system in children.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	molecular pathway suitable for targeting in the patient cohort by performing detailed genetic mapping and confirmatory analyses for markers and pathways identified through genome-wide association. (Target Met)			
SRO-3.10 By 2017, advance two candidate medications for treatment of substance use disorders to clinical studies in humans. (Outcome)	FY 2013: A pharmacogenetic study of the medication ondansetron revealed that variations in two different genes predict effectiveness in treating alcohol dependence. Target: Conduct pharmacogenetic studies to identify genetic variations that influence treatment response to one compound. (Target Met)	Conduct human laboratory studies on one candidate compound.	Conduct Phase 2 clinical testing of a novel compound	N/A
SRO-3.11 By 2017, advance the discovery of high need cures through innovations in the therapeutics discovery and development process, by developing 3-D human tissue chips that accurately model the structure and function of human organs. (Outcome)	FY 2013: All of the Tissue Chip for Drug Screening initiative grantees were funded for a second year, as they all either met or exceeded their milestones, and there was continued close collaboration with DARPA and FDA. Target: Initiate research on the therapeutics discovery and development process and "high need cures" projects. (Target Met)	Achieve progress towards early milestones for three collaborative "high need cures" projects.	Advance three projects to integration of individual organ or system chips into a multiple tissue chip or organ microsystem.	N/A
SRO-5.12 By 2013, identify several potential targets and/or molecules that modulate or enhance the extinction of learned behaviors and conditioned associations supporting addiction, compulsion, or anxiety	FY 2013: Compounds such as ceftriaxone, which regulates brain glutamate activity, and L822429, a neurokinin-1 receptor antagonist, have been shown to enhance extinction of drug-seeking behavior for cocaine and alcohol,	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
disorders. (Outcome)	respectively, and new data show that these compounds may also reduce relapse in animals self-administering other drugs of abuse such as nicotine (ceftriaxone) and alcohol (L822429). Target: Test whether compounds that have been shown to affect the extinction of drug seeking behavior for some drugs of abuse are equally effective against other drugs of abuse. (Target Met)			
SRO-5.13 By 2015, establish and evaluate a process to prioritize compounds that have not yet been adequately tested for more in-depth toxicological evaluation. (Outcome)	FY 2013: The 10,000 compound library was screened in 33 qHTS assays and data was analyzed on 179 compounds screened for cytotoxicity across 1086 human lymphoblastoid cell lines representing 9 racial groups to assess genetic diversity in response to toxicants. Target: Test 10,000 compound main library in 25 qHTS and test 180 compounds in densely sequenced human lymphoblastoid cell lines to assess genetic diversity in response to toxicants. (Target Met)	Test 10,000 compound main library in an additional 15 qHTS and test 20 subsets of possible high risk chemicals in high-content screens.	A formal process of prioritizing compounds for more extensive toxicological testing will be evaluated and used	N/A
SRO-5.14 By 2013, reduce tobacco prevalence among youth by preventing initiation and increasing rates of cessation. (Outcome)	FY 2013: NIH identified evidence-based strategies to reduce tobacco prevalence among low income youth and adult populations. Smokefree Teen (teen.smokefree.gov) provides youth with evidence-based tools,	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	resources, and strategies for tobacco cessation. Target: Identify best evidence-based strategies to reduce tobacco prevalence among youth by preventing initiation and increasing rates of cessation. (Target Met)			
SRO-5.15 By 2018, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance use, abuse, addiction and their consequences in underage populations. (Outcome)	(Will begin reporting in December 2014) (In Progress)	Develop materials to help academic officials address underage and harmful drinking and other substance use by their students.	Evaluate the effectiveness of screening and brief intervention for alcohol and other drug use in a variety of settings.	N/A
SRO-6.4 By 2015, identify and characterize two molecular pathways of potential clinical significance that may serve as the basis for discovering new medications for preventing and treating asthma exacerbations. (Outcome)	FY 2013: The Severe Asthma Research Program is conducting investigations. Target: Conduct investigations to elucidate the dynamic, pathophysiologic phenotypes of severe asthma. (Target Met)	Investigate the disease processes involved in asthma exacerbations and/or severe asthma using state-of-the-art pulmonary imaging techniques.	Identify and characterize two molecular pathways of potential clinical significance that may serve as the basis for discovering new medications for preventing and treating asthma exacerbations.	N/A
SRO-6.5 By 2014, develop and evaluate two new interventions for the prevention and/or treatment of HIV disease utilizing the newly restructured HIV/AIDS clinical trials networks. (Outcome)	FY 2013: The Vaginal and Oral Interventions to control the Epidemic (VOICE) study (MTN 003) to compare the safety and acceptability and efficacy of oral pre-exposure prophylaxis (PrEP) and topical microbicides for prevention of sexual transmission of HIV in women was completed. Target: Complete the first study to compare the safety,	Evaluate non-tenofovir based strategies for HIV pre-exposure prophylaxis (PrEP) in men who have sex with men and women who are at increased risk of HIV infection in the U.S. In addition,	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	acceptability and efficacy of oral pre-exposure prophylaxis (PrEP) and topical microbicides for prevention of sexual transmission of HIV in women. (Target Met)	complete an evaluation of a comprehensive test, link, and care "plus" strategy for HIV prevention in New York City, Washington, DC, and four comparator cities in the U.S.		
SRO-6.6 By 2015, provide at least one new or significantly improved minimally-invasive treatment for clinical use in patients using image-guided interventions. (Outcome)	FY 2013: Development was completed on image guided interventions for assessing involvement of lymph nodes in cancer, skin cancer and for the treatment of cardiac arrhythmias. Target: Conduct one additional feasibility study on new IGI technologies for the diagnosis of lymph node cancer, treatment of skin cancer, and treatment of cardiac arrhythmias. (Target Met)	Identify how the use of a new or emerging IGI technology affects physician performance, or what physician training is necessary.	Support new or significantly improved human subject research for image-guided interventions to reduce the risk of adverse outcomes to structures such as the brain, spinal cord, or nerves that are within or near the operating field.	N/A
SRO-7.11 (RA) By 2013, gather sufficient data to support the development of a national standard for normal fetal growth. (Outcome)	FY 2013: The data management structure accepted imaging data and data collection to support a national standard for normal fetal growth is complete. Target: Complete data collection to support the development of a national standard for normal fetal growth. (Target Met)	N/A	N/A	N/A
SRO-8.7 By 2018, identify three effective system interventions generating the implementation,	FY 2013: NIH researchers identified three influences on sustainability of research-tested interventions in service systems such as	Identify three effective implementation strategies that enhance the	Identify three (3) key factors influencing the scaling up of research-tested	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
sustainability and ongoing improvement of research-tested interventions across health care systems. (Outcome)	primary care, specialty care, and community practice: Community Development Teams in child mental health service systems; barriers and facilitators to evidence-based interventions to control blood pressure in community practice; and a set of factors to enhance sustainability of health care interventions across multiple settings. Target: Identify three key factors influencing the sustainability of research-tested interventions in service systems such as primary care, specialty care, and community practice. (Target Met)	sustainability of research-tested interventions in service systems such as primary care, specialty care and community practice.	interventions across large networks of services systems such as primary care, specialty care and community practice. (Outcome)	
SRO-8.9 By 2014, identify 12 pathogen and/or host factors critical for understanding the molecular and cellular basis of pathogenesis of Category A-C biodefense pathogens and/or pathogens causing emerging infectious diseases. (Outcome)	FY 2013: Twenty pathogens and/or host factors, including those that cause: dengue, hepatitis, TB, SARS, influenza, Marburg, E. coli, tularemia, Burkholderia infection, Rift Valley Fever, plague, arenavirus infection, Q fever, rabies, smallpox, botulism, were identified that are critical for understanding pathogenesis and show promise for the development of new therapeutics. Target: Identify three pathogens and/or host factors. (Target Exceeded)	Identify four pathogen and/or host factors.	N/A	N/A
SRO-9.2 By 2018, identify culturally appropriate, effective stroke prevention/intervention programs in minority	FY 2013: Completed testing of a culturally tailored intervention in an underserved minority community and demonstrated an increased	Develop a protocol for testing a new prevention and/or intervention	Initiate enrollment in two studies testing culturally tailored interventions to	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
communities. (Outcome and Efficiency)	proportion of patients with acute stroke who arrived at the hospital rapidly and were treated with tissue plasminogen activator. Target: Complete testing of a culturally tailored intervention to improve stroke awareness and time to hospital arrival in order to increase utilization of tissue plasminogen activator (tPA) treatment in minority populations. (Target Met)	program that aims to reduce a major cause of disparities in stroke in minority communities.	reduce health disparities in stroke.	
SRO-9.4 By 2014, develop and evaluate the efficacy of neonatal screening for congenital cytomegalovirus (CMV) infection to permit identification of infants who will develop CMV-induced hearing loss in the first years of life. (Outcome)	FY 2013: An interim report on the longitudinal study of infants infected with CMV determined that 6.3% of infants born infected with CMV yet with no clinical symptoms will develop hearing loss in the first years of life. Target: Provide an interim report on how many children identified with neonatal asymptomatic CMV-infection have developed hearing loss. (Target Met)	Develop and evaluate the efficacy of neonatal screening for congenital cytomegalovirus (CMV) infection to permit identification of infants who will develop CMV-induced hearing loss in the first years of life.	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
SRO-9.5 By 2015, assess the efficacy of long-term oxygen treatment in patients with COPD and moderate hypoxemia. (Outcome)	FY 2013: LOTT recruited 643 participants. Target: Continue recruitment to 626 subjects. (Target Met)	Complete recruitment (737 total subjects).	Complete data analysis and publish results of study assessing the efficacy of long-term oxygen treatment in patients with COPD and moderate hypoxemia.	N/A
CBRR-1.1 Provide research training for predoctoral trainees and fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2013: Award rate to comparison group reached 11%. Target: N > 10% (Target Met)	N > 10%	N > 10%	N/A
CBRR-1.2 Provide research training for postdoctoral fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2013: Award rate to comparison group reached 13% and exceeded the target by 3%. Target: N > 10% (Target Met)	N > 10%	N > 10%	N/A
CBRR-2 Promote data sharing and provide information in real time through the NIH Business System (NBS) by developing, integrating, deploying and maintaining business modules. (By FY 2014, the NBS will be in an ongoing status) (Output)	FY 2013: Maintained post deployment support for Animal Procurement. Target: (Maintenance [Mat]) Maintain deployed business modules. * Planned - Service and Supply Activities Fund Module [Dep.2012] *Planned - Animal Procurement [Dep. 2013] (Target Met) FY 2013: Deployed Animal Procurement. Target: (Deployment [Dep])	Development [Dev]) Initiate development of planned business modules to build capacity and functionality of the NIH Business System. * Planned - Oracle 12i Upgrade [continuation from Dev. start in 2012, thru 2015/Int.2015-16]	Development [Dev]) Initiate development of planned business modules to build capacity and functionality of the NIH Business System. * Planned - Oracle 12i Upgrade [continuation from 2014/Int.2015-16] (Integration	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	Conduct priority deployment activities to enable user accessibility and skill development within 2 years from the onset of integration. * Planned - Animal Procurement (Target Met) FY 2013: Completed integration for Animal Procurement. Target: (Integration [Int]) Complete integration activities for full functionality and usability of priority modules for successful development efforts within 3 years of initiated development. * Planned - Animal Procurement [Dev.2013/Dep.2014] (Target Met) FY 2013: Initiated development of Animal Procurement. Target: (Development [Devl]) Initiate development of planned business modules to build capacity and functionality of the NIH Business System.* Planned - Animal Procurement [Int.2013] (Target Met)		[Int]) Complete integration activities for full functionality and usability of priority modules for successful development efforts within 3 years of development. * Planned - Oracle 12i Upgrade [Dev.2012, 2014-15/Dep.2016]	
CBRR-6.2 By 2013 complete construction/commissioning of 15 biocontainment facilities to support biodefense and emerging infectious disease	FY 2013: The Regional Biocontainment Laboratory (RBL) project at the University of Hawaii has been suspended by the University and the orderly closeout of the project,	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
research needs, including research on Category A-C Priority agents and newly emerging infectious diseases. (Output)	including the return of funds to the Federal government, is in process. Early in the planning process, the University had challenges securing the required matching funds for construction; ultimately, its inability to secure a viable site for construction caused the demise of the project, despite significant attempts by NIH to provide assistance. Target: Conduct design development Previous target: Begin construction on final research facility. (Target Not Met)			
CBRR-10 Make freely available to researchers the results of 400 high-throughput biological assays screened against a library of 300,000 unique compounds, and the detailed information on the molecular probes that are developed through that screening process. (Outcome)	FY 2013: Established 570 primary biochemical, cell-based or protein-protein interaction assays that were miniaturized and automated as high throughput screens in the Molecular Libraries Program (MLP) Portfolio. Target: Establish 400 primary biochemical, cell-based or protein-protein interaction assays that can be miniaturized and automated as high throughput screens in the Molecular Libraries Program (MLP) Portfolio. (Target Exceeded)	Increase the Molecular Libraries Program (MLP) inventory to 375 small molecule probes that can be used in biological research to interrogate basic biological processes or disease.	Make freely available to researchers the results of 400 high-throughput biological assays screened against a library of 300,000 unique compounds, and the detailed information on the molecular probes that are developed through that screening process.	N/A
CTR-1 By 2014, reduce the disparity between African American and white infants in back sleeping by 50% to further reduce the risk of sudden infant death syndrome (SIDS). (Outcome and Efficiency)	FY 2013: The NIH successfully conducted three meetings with up to nine federal agencies in attendance to determine outreach strategies to reduce the number African American infants who die from SIDS.	Conduct a SIDS risk-reduction training workshop at the National Baptist Convention's annual meeting session, which has an	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	Target: Convene two meetings with two or more federal agencies on how to coordinate efforts to reduce SIDS in African American communities across the nation. (Target Exceeded)	attendance of approximately 10,000 African American church delegates from across the country.		
CTR-10 By 2014, expand the scope of the Hazardous Substances Data Bank to include 14 nanomaterials. (Outcome)	FY 2014: The Hazardous Substances Data Bank was augmented to include 14 nanomaterials. Target: Augment the Hazardous Substances Data Bank with comprehensive records for 5 nanomaterials. (Target Met) Measure achieved earlier than anticipated.	Augment the Hazardous Substances Data Bank with comprehensive records for 5 nanomaterials.	N/A	N/A
POI-2 Utilize performance-based contracting (PBC). (ongoing) (Output)	FY 2013: Obligated 38% of eligible service contracting dollars through performance-based contracting. Target: Obligate the FY 2013 OMB/OFPP goal of eligible service contracting dollars to PBC. (Target Not Met)	Obligate the FY 2014 OMB/OFPP goal of eligible service contracting dollars to PBC.	Obligate the FY 2015 OMB/OFPP goal of eligible service contracting dollars to PBC.	N/A
POI-6.1 Improve facility conditions in order to reach and maintain a Condition Index (CI) weighted average of 85 or above (CIwa≥85).	FY 2013: The condition of the facilities portfolio reached a CIwa of 80.96. Target: CIwa = 75.4 (Target Exceeded)	CIwa = 72.1	CIwa = 79.9	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
POI-6.2 By 2017, maintain the annual condition of buildings and facilities portfolio so that no less than 95% of occupied gross square feet (GSF) will have a CI greater than 65.	FY 2013: 73% of occupied gross square feet (GSF) reached a CI greater than 65. Target: 69.6% (Target Exceeded)	73.1%	73.5%	N/A
POI-7.1 Manage all Buildings and Facilities (B&F) line item projects so it is completed within 100% of the final approved project cost	FY 2013: The eight (8) active Recovery Act funded projects at the HHS Facility Project Approval Agreement (FPAA) threshold were managed effectively to ensure completion within 100% of the final approved project cost. Target: (2013 RA) 8 Active Recovery Act projects (Target Met) FY 2013: Nine (9) of the twelve (12) active non-Recovery Act funded projects at the HHS Facility Project Approval Agreement (FPAA) level threshold were effectively managed to ensure completion within 100% of the final approved project cost. Target: 12 Active Projects (Target Not Met)	12 Active Projects 3 Active Recovery Act projects	11 Active Projects 1 Active Recovery Act projects	N/A
POI-7.2 Manage design and construction of capital facility projects funded by B&F so that no more than 10% of the projects may incorporate plus or minus 10% adjustments of the approved scope	FY 2013: The design and construction of the eight (8) active reportable Recovery Act funded projects was managed effectively so that no more than 10% of the projects incorporated a plus or minus 10% adjustment of	12 Active Projects 3 Active Recovery Act projects	11 Active Projects 1 Active Recovery Act projects	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	the approved scope. Target: (2013 RA) 8 Active Recovery Act funded Project (Target Met) FY 2013: The design and construction of ten (10) of the twelve (12) active non-Recovery Act funded projects was managed effectively so that no more than 10% of the projects incorporated a plus or minus 10% adjustments of the approved scope. One (1) project was canceled and the work incorporated under another project for costs savings. Another project was delayed to support further analysis of the most viable programmatic and facilities solution. Target: 12 Active Projects (Target Not Met)			
POI-8.1 By 2013, ensure that 100% of grantees have met all construction requirements, including NIH approved design and construction documents that ensures proposed research in the space is feasible, and ensures that grantees will take action to file or record a Notice of Federal Interest that ensures grantees cannot lease, sell or mortgage property without NIH approval. (Output)	FY 2013: Of the remaining ARRA awarded grantes, one grant was unable to complete all documents due to the devastation of Hurricane Sandy. Target: Ensure that 100% of 79 grantees have met all construction requirements. (Target Not Met)	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
POI-8.2 By 2015, report the percent of extramural construction projects that are in compliance with the post award 20 year usage requirement to conduct research. (Output)	FY 2013: 99% of the extramural construction projects were in compliance with the post award 20 years usage requirement. Target: 95% of 219 projects are in compliance. (Target Met)	95% of 196 projects are in compliance.	95% of 212 projects are in compliance	N/A
POI-9 Reallocate laboratory resources based on external reviews by Boards of Scientific Counselors. (Output)	FY 2013: 25% of Principal Investigators were reviewed resulting in 25% of resources recommended to be reallocated Target: Conduct BSC reviews of 25% of Principal Investigators to assess quality of science in order to prioritize of resources. (Target Met)	Conduct BSC reviews of 25% of principal Investigators to assess quality of science in order to prioritize resources.	Conduct BSC reviews of 25% of principal Investigators to assess quality of science in order to prioritize resources.	N/A
SMHC-6 Provide opportunities for enhanced leadership skills to meet the challenges of workforce management and/or individual advancements. (Ongoing) (Output)	FY 2013: NIH reviewed literature and benchmarked other organizations to determine best practices in delivering executive coaching programs in the public sector and determine principles around which to operate the internal program. Target: Examine [EX] key area to enhance leadership skills. * Study best practices in implementing and evaluating executive coaching programs in the federal sector. [IM 2014] (Target Exceeded) FY 2013: NIH implemented recommendations from the previous year to offer a multifaceted program of	Examine [EX] key area to enhance leadership skills * Study NIH's administrative intern and fellows program to determine if there are improvements, efficiencies, or additional best practices that can enhance long-standing programs intended to recruit and develop the best and the brightest for future NIH leadership roles. [IM 2015]	Assess [AS] results of implementation * Assess results from implementing best practices in implementing and evaluating executive coaching programs in the federal sector. [IM 2014/EX2013] Implement [IM] recommendation from prior year assessments * Implement recommendations from study of NIH's	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	supervisory training geared towards meeting both the basic requirements of all new supervisors and the more varied needs of all existing supervisors. Target: Implement [IM] recommendation from prior year assessments. * Create and implement revised supervisory training. [EX.2012/AS.2014] (Target Exceeded) FY 2013: The Executive Onboarding Program analyzed the effectiveness of retaining employees. All new hires who participated remain at NIH, and every new executive continues to receive onboarding through the program. Target: Assess [AS] results of implementation. * Assess results from executive on-boarding program. [IM 2012] (Target Exceeded)	Implement [IM] recommendation from prior year assessments * Implement best practices in implementing and evaluating executive coaching programs in the federal sector. [AS 2013] Assess [AS] results of implementation * Assess results from revised supervisory training. [IM 2013]	administrative intern and fellows program [EX 2014/ AS 2016] Examine [EX] key area to enhance leadership skills * Assess best practices and review the literature regarding incorporating the latest technologies into leadership development programs to determine which are most effective and practicable to create efficiencies and/or enhance learning [IM 2016/ AS 2017]	
SMHC-7 Address diverse workforce recruitment needs to ascertain highly qualified staff to conduct or support biomedical research. (Ongoing) (Output)	FY 2013: NIH developed a corporate recruitment strategy for FY13 enhancing partnerships, connecting talent, and streamlined pathways program recruitment. SMRF FY13 executed pilot "Career Experience Program" and Discover a Career initiative. Target: Implement [IM] key area to enhance recruitment *Develop corporate recruitment strategy to focus on diversity recruiting, student recruiting, and trans-	Implement [IM] key area to enhance recruitment *Increase oversight and review of Title 42 recruitment. [EX 2013] [AS 2015] Implement [IM] key area to enhance recruitment *Increase participation in	Assess [AS] results of implementation *Create the Scientific and Medical Recruitment Forum (SMRF) to attract world-class scientists and medical professionals to drive discovery and innovation at NIH. [IM 2014]	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2014 Target	FY 2015 Target	FY 2015 Target +/-FY 2014 Target
	NIH hiring. [EX 2012] [AS 2014] *Create the Scientific and Medical Recruitment Forum (SMRF) to attract world-class scientists and medical professionals to drive discovery and innovation at NIH. [IM 2014] [AS 2015] (Target Met) FY 2013: Expanded the use of Pathways recruitments for the scientific community. Implemented and managed automated register and applicant referral process for management selection of candidates. Target: Examine [EX] key area to enhance recruitment *Implement Pathways Program to establish a focused student and entry level recruitment plan that supports succession planning efforts at NIH. [IM 2014] [AS 2015] (Target Met) FY 2013: NIH has developed an action plan to identify ways to enhance oversight and management of Title 42 cases and new procedures for exhaustion. In addition NIH is developing training on preparing cases. Target: Examine [EX] key area to enhance recruitment *Establish increased oversight and review of Title 42 recruitment. [IM 2014] [AS 2015] (Target Met)	Pathways Program to promote a focused student and entry level recruitment plan that supports succession planning efforts at NIH. [EX 2013] [AS 2015] Assess [AS] results of implementation and [IM] implement key areas to enhance recruitment *Evaluate corporate recruitment strategies: diversity and student recruiting, and trans-NIH hiring. [EX 2012] [IM 2013] *Develop the Scientific and Medical Recruitment Forum (SMRF) to continue attracting world-class scientists and medical professionals to drive discovery and innovation at NIH. [EX	Assess [AS] results of implementation *Implement Pathways Program to establish a focused student and entry level recruitment plan that supports succession planning efforts at NIH. [IM 2014] Assess [AS] results of implementation *Establish increased oversight and review of Title 42 recruitment. [IM 2014] Examine [EX] key area to enhance recruitment *Increase the use of Global Recruitments. [IM 2016] [AS 2017] Examine [EX] key area to enhance recruit *Launch a robust OHR succession planning effort to ensure OHR staff are available to meet the recruitment needs of NIH. [IM 2016] [AS 2017]	

Supplementary Tables

Department of Health and Human Services

National Institutes of Health

Supplementary Tables

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Budget Request by Institute/Center
(Dollars in Thousands)

Institute/Center	FY 2013 Actual [1, 2]	FY 2014 Enacted [2]	FY 2015 President's Budget
NCI	$4,783,442	$4,922,771	$4,930,715
NHLBI	2,900,321	2,982,737	2,987,685
NIDCR	386,874	397,102	397,131
NIDDK [3]	1,692,748	1,741,874	1,743,336
NINDS	1,531,975	1,585,797	1,608,461
NIAID:	4,230,080	4,392,670	4,423,357
NIGMS	2,290,525	2,361,894	2,368,877
NICHD	1,244,707	1,280,830	1,283,487
NEI	656,291	674,249	675,168
NIEHS [4]	645,782	664,524	665,080
NIA	1,039,399	1,169,427	1,170,880
NIAMS	504,691	519,338	520,189
NIDCD	392,113	403,493	403,933
NIMH	1,394,354	1,416,825	1,440,076
NIDA	992,232	1,015,754	1,023,268
NIAAA	432,849	445,411	446,017
NINR	136,367	140,324	140,452
NHGRI	483,107	497,128	498,451
NIBIB	318,720	326,359	328,532
NIMHD	260,396	267,953	267,953
NCCAM	120,624	124,125	124,509
NCATS	541,973	632,396	657,471
FIC	65,581	67,484	67,776
NLM	352,268	367,223	372,851
OD	1,410,515	1,399,753	1,451,786
B&F	118,109	128,663	128,663
Subtotal, Labor/HHS Discretionary Budget Authority	**$28,926,041**	**$29,926,104**	**$30,126,104**
Superfund (Interior)	74,871	77,349	77,349
Total, Discretionary Budget Authority	**$29,000,912**	**$30,003,453**	**$30,203,453**
Type 1 Diabetes	142,350	139,200	150,000
Total, Budget Authority	**$29,143,262**	**$30,142,653**	**$30,353,453**
NLM Program Evaluation	8,200	8,200	8,200
Total, Program Level	**$29,151,462**	**$30,150,853**	**$30,361,653**

[1] Includes effect of sequestration and transfers.

[2] FY 2013 and FY 2014 figures are shown on a comparable basis to FY 2015, reflecting the NCBI and PA proposal.

[3] Excludes amount for Type 1 Diabetes.

[4] Excludes amount allocated for Superfund Research activities from Interior, Environment, and Related Agencies appropriation.

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Budget Authority: Appropriations Adjustments for FY 2013
(Dollars in Thousands)

		FY 2013 Transfers				FY 2013 Comparable Adjustments		
IC	**FY 2013 Budget Authority**	**Type 1 Diabetes**	**Sec. Transfers**	**NCS Transfers**	**HIV/AIDS Transfers**	**Subtotal B.A.**	**NCBI and PA**	**Comparable Budget Authority**
NCI	$4,807,450		-$28,044	$4,077	$5,637	$4,789,120	-$5,678	$4,783,442
NHLBI	2,918,317		-17,024	2,475	-	2,903,768	-3,447	2,900,321
NIDCR	389,274		-2,271	330	-	387,333	-460	386,874
NIDDK	1,703,251	142,350	-9,936	1,444	-	1,837,109	-2,012	1,835,098
NINDS	1,541,480		-8,992	1,307	-	1,533,795	-1,821	1,531,975
NIAID	4,256,327		-24,829	3,609	-	4,235,107	-5,027	4,230,080
NIGMS	2,303,204		-11,910	1,953	-	2,293,248	-2,722	2,290,525
NICHD	1,252,430		-7,306	1,062	-	1,246,186	-1,479	1,244,707
NEI	666,036		-3,885	565	-5,637	657,078	-787	656,291
NIEHS	649,789		-3,791	551	-	646,550	-767	645,782
NIA	1,045,849		-6,101	887	-	1,040,634	-1,235	1,039,399
NIAMS	507,822		-2,962	431	-	505,290	-600	504,691
NIDCD	394,546		-2,302	335	-	392,579	-466	392,113
NIMH	1,403,005		-8,184	1,190	-	1,396,011	-1,657	1,394,354
NIDA	998,389		-5,824	847	-	993,411	-1,179	992,232
NIAAA	435,535		-2,541	369	-	433,364	-514	432,849
NINR	137,213		-800	116	-	136,529	-162	136,367
NHGRI	486,104		-2,836	412	-	483,681	-574	483,107
NIBIB	320,697		-1,871	272	-	319,099	-379	318,720
NIMHD	262,011		-1,528	222	-	260,705	-309	260,396
NCCAM	121,373		-708	103	-	120,768	-143	120,624
NCATS	545,336		-3,181	462	-	542,618	-644	541,973
FIC	65,988		-385	56	-	65,659	-78	65,581
NLM	320,016		-1,867	271	-	318,421	33,847	352,268
OD	1,448,420		-12,790	-23,410	-	1,412,220	-1,706	1,410,515
B&F	118,802		-693	-	-	118,109	-	118,109
Total NIH	**$29,098,666**	**$142,350**	**-$172,561**	**-$63**	-	**$29,068,391**	-	**$29,068,391**
Superfund	74,808			63		74,871		74,871
Total, B.A.	**$29,173,474**	**$142,350**	**-$172,561**	-	-	**$29,143,262**	-	**$29,143,262**
NLM Pgm. Eval.	$8,200					$8,200		$8,200
Total Pgm. Level	**$29,181,674**	**$142,350**	**-$172,561**	-	-	**$29,151,462**	-	**$29,151,462**

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Budget Authority: Appropriations Adjustments for FY 2014
(Dollars in Thousands)

		FY 2014 Transfers		FY 2014 Comparable Adjustments		
IC	FY 2014 Enacted	Type 1 Diabetes	HIV/AIDS Transfers	Subtotal B.A.	NCBI and PA	Comparable Budget Authority
NCI	$4,923,238		$6,307	$4,929,545	-$6,774	$4,922,771
NHLBI	2,988,605		-1,756	$2,986,849	-4,112	2,982,737
NIDCR	398,650		-1,000	$397,650	-548	397,102
NIDDK	1,744,274	139,200	-	$1,883,474	-2,400	1,881,074
NINDS	1,587,982		-	$1,587,982	-2,185	1,585,797
NIAID	4,358,841		39,826	$4,398,667	-5,997	4,392,670
NIGMS	2,364,147		1,000	$2,365,147	-3,253	2,361,894
NICHD	1,282,595		-	$1,282,595	-1,765	1,280,830
NEI	682,077		-6,890	$675,187	-938	674,249
NIEHS	665,439		-	$665,439	-915	664,524
NIA	1,171,038		-	$1,171,038	-1,611	1,169,427
NIAMS	520,053		-	$520,053	-715	519,338
NIDCD	404,049		-	$404,049	-556	403,493
NIMH	1,446,172		-27,357	$1,418,815	-1,990	1,416,825
NIDA	1,025,435		-8,270	$1,017,165	-1,411	1,015,754
NIAAA	446,025		-	$446,025	-614	445,411
NINR	140,517		-	$140,517	-193	140,324
NHGRI	497,813		-	$497,813	-685	497,128
NIBIB	329,172		-2,360	$326,812	-453	326,359
NIMHD	268,322		-	$268,322	-369	267,953
NCCAM	124,296		-	$124,296	-171	124,125
NCATS	633,267		-	$633,267	-871	632,396
FIC	67,577		-	$67,577	-93	67,484
NLM	327,723		500	$328,223	39,000	367,223
OD	1,400,134		-	$1,400,134	-381	1,399,753
B&F	128,663		-	$128,663	-	128,663
Total NIH	**$29,926,104**	**$139,200**	-	**$30,065,304**	-	**$30,065,304**
Superfund	77,349			77,349		77,349
Total, B.A.	**$30,003,453**	**$139,200**	-	**$30,142,653**	-	**$30,142,653**
NLM Pgm. Eval.	8,200			$8,200		$8,200
Total Pgm. Level	**$30,011,653**	**$139,200**	-	**$30,150,853**	-	**$30,150,853**

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Budget Mechanism - Total

(Dollars in Thousands)

MECHANISM	FY 2013 Actual [2]		FY 2014 Enacted [2,3]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	25,140	$11,119,346	23,632	$10,959,764	23,236	$11,198,737	-396	$238,973
Administrative Supplements	*(1,315)*	248,370	*(1,215)*	154,272	*(1,204)*	149,179	*(-11)*	-5,093
Competing:								
Renewal	1,766	904,567	2,006	1,280,732	1,960	956,371	-46	-324,361
New	6,419	2,525,738	6,950	2,977,247	7,322	3,167,151	372	189,904
Supplements	49	8,926	41	8,231	44	8,788	3	557
Subtotal, Competing	8,234	$3,439,230	8,997	$4,266,210	9,326	$4,132,310	329	-$133,900
Subtotal, RPGs	33,374	$14,806,946	32,629	$15,380,246	32,562	$15,480,226	-67	$99,980
SBIR/STTR	1,466	638,517	1,584	697,086	1,635	716,621	51	19,535
Research Project Grants	34,840	$15,445,463	34,213	$16,077,332	34,197	$16,196,847	-16	$119,515
Research Centers:								
Specialized/Comprehensive	1,177	$1,994,721	1,128	$1,960,307	1,149	$1,962,737	21	$2,430
Clinical Research	58	370,187	58	407,107	58	402,021	0	-5,086
Biotechnology	89	156,159	88	157,710	90	170,682	2	12,972
Comparative Medicine	52	132,623	52	132,864	52	132,327	0	-537
Research Centers in Minority Institutions	21	55,055	21	55,067	21	55,067	0	0
Research Centers	1,397	$2,708,745	1,347	$2,713,055	1,370	$2,722,834	23	$9,779
Other Research:								
Research Careers	3,677	$614,651	3,715	$625,157	3,710	$626,778	-5	$1,621
Cancer Education	96	34,466	96	35,500	96	36,561	0	1,061
Cooperative Clinical Research	431	434,870	492	456,827	492	463,979	0	7,152
Biomedical Research Support	122	69,214	88	64,588	88	64,432	0	-156
Minority Biomedical Research Support	310	104,656	313	104,927	316	105,146	3	219
Other	1,748	525,628	1,778	537,799	1,804	571,083	26	33,284
Other Research	6,384	$1,783,484	6,482	$1,824,798	6,506	$1,867,979	24	$43,181
Total Research Grants	42,621	$19,937,692	42,042	$20,615,185	42,073	$20,787,660	31	$172,475
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,071	$132,034	3,126	$138,879	3,195	$141,865	69	$2,986
Institutional Awards	12,468	601,489	12,481	613,998	12,520	625,267	39	11,269
Total Research Training	15,539	$733,524	15,607	$752,877	15,715	$767,132	108	$14,255
Research & Develop. Contracts	2,339	$2,895,302	2,210	$2,990,346	2,186	$3,030,746	-24	$40,400
(SBIR/STTR) (non-add) [1]	*(120)*	*(59,137)*	*(127)*	*(64,982)*	*(127)*	*(70,995)*	*(0)*	*(6,013)*
Intramural Research	7,126	$3,282,734	7,137	$3,395,910	7,137	$3,435,324	0	$39,414
Res. Management & Support	5,580	1,485,463	5,697	1,528,653	5,697	1,544,027	0	15,374
Res. Management & Support (SBIR Admin) (non-add) [1]	*(2)*	*(3,185)*	*(10)*	*(6,084)*	*(10)*	*(5,934)*	*0*	*(-150)*
Office of the Director								
OD - Other		607,663		572,519		574,552		2,033
OD Common Fund (non-add) [1, 4]		*(513,476)*		*(533,039)*		*(583,039)*		*(50,000)*
ORIP/SEPA (non-add) [1, 4]		*(289,376)*		*(294,195)*		*(294,195)*		*(0)*
OD Appropriation (non-add) [1,4]		*(1,410,515)*		*(1,399,753)*		*(1,451,786)*		*(52,033)*
Buildings and Facilities[5]		126,013		136,341		136,663		322
Appropriation [1]		*(118,109)*		*(128,663)*		*(128,663)*		0
Type 1 Diabetes[6]		-142,350		-139,200		-150,000		-10,800
Subtotal, Labor/HHS Budget Authority		**$28,926,041**		**$29,926,104**		**$30,126,104**		**$200,000**
Interior Appropriation for Superfund Res.		74,871		77,349		77,349		0
Total, NIH Discretionary B.A.		**$29,000,912**		**$30,003,453**		**$30,203,453**		**$200,000**
Type 1 Diabetes		142,350		139,200		150,000		10,800
Total, NIH Budget Authority		**$29,143,262**		**$30,142,653**		**$30,353,453**		**$210,800**
NLM Program Evaluation		8,200		8,200		8,200		0
Total, Program Level		**$29,151,462**		**$30,150,853**		**$30,361,653**		**$210,800**

[1] All items in italics and brackets are non-add.

[2] FY 2013 and FY 2014 figures are shown on a comparable basis to FY 2015, reflecting the NCBI and PA proposal.

[3] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

[4] Number of grants and dollar amounts 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 under OD-Other.

[5] Includes B&F appropriation plus building repair and improvement (R&I) dollars appropriated to NCI for the Frederick MD facility.

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

NATIONAL INSTITUTES OF HEALTH

FY 2015 Budget Authority by Object Class Including Type I Diabetes Funds*

(Dollars in Thousands)

Object Classes	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Personnel Compensation			
Full-Time Permanent (11.1)	$916,625	$927,274	$10,649
Other Than Full-Time Permanent (11.3)	467,330	472,629	5,299
Other Personnel Compensation (11.5)	19,332	19,538	206
Military Personnel (11.7)	21,276	21,513	237
Special Personnel Services Payments (11.8)	160,140	161,758	1,618
Subtotal Personnel Compensation (11.9)	**$1,584,703**	**$1,602,712**	**$18,010**
Civilian Personnel Benefits (12.1)	428,765	443,797	15,031
Military Personnel Benefits (12.2)	14,770	14,925	154
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,028,239**	**$2,061,434**	**$33,195**
Travel & Transportation of Persons (21.0)	45,097	45,225	128
Transportation of Things (22.0)	5,164	5,180	15
Rental Payments to GSA (23.1)	1,697	1,703	5
Rental Payments to Others (23.2)	483	490	6
Communications, Utilities & Misc. Charges (23.3)	29,064	29,150	86
Printing & Reproduction (24.0)	1,059	948	-111
Consultant Services (25.1)	114,040	115,214	1,175
Other Services (25.2)	829,401	804,266	-25,135
Purchase of goods and services from government accounts (25.3)	2,945,974	2,998,474	52,499
Operation & Maintenance of Facilities (25.4)	173,948	175,812	1,864
R&D Contracts (25.5)	2,191,969	2,171,703	-20,266
Medical Care (25.6)	21,937	22,088	152
Operation & Maintenance of Equipment (25.7)	108,196	109,378	1,182
Subsistence & Support of Persons (25.8)	0	-16	-16
Subtotal Other Contractual Services (25.0)	**$6,385,465**	**$6,396,920**	**$11,454**
Supplies & Materials (26.0)	182,553	183,133	580
Equipment (31.0)	135,182	136,568	1,385
Land and Structures (32.0)	33	33	0
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	21,251,257	21,415,311	164,055
Insurance Claims & Indemnities (42.0)	0	0	0
Interest & Dividends (43.0)	11	11	0
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$28,037,065**	**$28,214,670**	**$177,605**
Total Budget Authority	**$30,065,304**	**$30,276,104**	**$210,800**

* Excludes Superfund Research account under the jurisdiction of the Interior, Environment & Related Agencies Appropriations Subcommittee. PHS Evaluation Fund allocation to NLM also excluded.

NATIONAL INSTITUTES OF HEALTH

FY 2015 Budget Authority by Object Class Including Service and Supply Fund and Management Fund*

(Dollars in Thousands)

Object Classes	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Personnel Compensation			
Full-Time Permanent (11.1)	$1,239,437	$1,251,696	$12,259
Other Than Full-Time Permanent (11.3)	562,188	568,423	6,235
Other Personnel Compensation (11.5)	38,199	38,534	335
Military Personnel (11.7)	29,925	30,226	300
Special Personnel Services Payments (11.8)	164,769	166,431	1,662
Subtotal Personnel Compensation (11.9)	**$2,034,518**	**$2,055,309**	**$20,791**
Civilian Personnel Benefits (12.1)	554,088	569,824	15,736
Military Personnel Benefits (12.2)	20,405	20,582	177
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,609,011**	**$2,645,715**	**$36,704**
Travel & Transportation of Persons (21.0)	47,282	47,426	144
Transportation of Things (22.0)	6,699	6,718	19
Rental Payments to GSA (23.1)	69,990	70,007	18
Rental Payments to Others (23.2)	98,410	98,416	6
Communications, Utilities & Misc. Charges (23.3)	146,975	147,061	86
Printing & Reproduction (24.0)	3,040	2,928	-111
Consultant Services (25.1)	283,053	284,228	1,175
Other Services (25.2)	1,115,363	1,091,624	-23,739
Purchase of goods and services from government accounts (25.3)	1,264,104	1,311,650	47,546
Operation & Maintenance of Facilities (25.4)	265,508	267,374	1,866
R&D Contracts (25.5)	2,192,943	2,172,677	-20,266
Medical Care (25.6)	26,338	26,490	152
Operation & Maintenance of Equipment (25.7)	208,766	209,948	1,182
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services (25.0)	**$5,356,079**	**$5,363,993**	**$7,913**
Supplies & Materials (26.0)	301,681	302,262	580
Equipment (31.0)	174,788	176,173	1,385
Land and Structures (32.0)	57	57	0
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	21,251,257	21,415,311	164,055
Insurance Claims & Indemnities (42.0)	5	5	0
Interest & Dividends (43.0)	32	32	0
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$27,456,293**	**$27,630,389**	**$174,096**
Total Budget Authority	**$30,065,304**	**$30,276,104**	**$210,800**

* Excludes Superfund Research account under the jurisdiction of the Interior, Environment & Related Agencies Appropriations Subcommittee. PHS Evaluation Fund allocation to NLM also excluded.

NATIONAL INSTITUTES OF HEALTH

FY 2015 Budget Authority by Object Class Including Type I Diabetes Funds[1]
Salaries and Expenses / Administrative Expenses
(Dollars in Thousands)

Object Classes	FY 2014 Enacted	FY 2015 President's Budget	FY 2014 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$916,625	$927,274	$10,649
Other Than Full-Time Permanent (11.3)	467,330	472,629	5,299
Other Personnel Compensation (11.5)	19,332	19,538	206
Military Personnel (11.7)	21,276	21,513	237
Special Personnel Services Payments (11.8)	160,140	161,758	1,618
Subtotal Personnel Compensation (11.9)	**$1,584,703**	**$1,602,712**	**$18,010**
Civilian Personnel Benefits (12.1)	428,765	443,797	15,031
Military Personnel Benefits (12.2)	14,770	14,925	154
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,028,239**	**$2,061,434**	**$33,195**
Travel & Transportation of Persons (21.0)	45,097	45,225	128
Transportation of Things (22.0)	5,164	5,180	15
Rental Payments to Others (23.2)	483	490	6
Communications, Utilities & Misc. Charges (23.3)	29,064	29,150	86
Printing & Reproduction (24.0)	1,059	948	-111
Other Contractual Services:			
Consultant Services (25.1) [2]	101,895	103,048	1,153
Other Services (25.2)	829,401	804,266	-25,135
Purchase of goods and services from government accounts (25.3) [2]	1,918,262	1,875,003	-43,259
Operation & Maintenance of Facilities (25.4) [2]	159,425	161,248	1,823
Operation & Maintenance of Equipment (25.7)	108,196	109,378	1,182
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$3,117,179**	**$3,052,943**	**-$64,236**
Supplies & Materials (26.0)	182,553	183,133	580
Subtotal Non-Pay Costs	**$3,380,599**	**$3,317,068**	**-$63,531**
Total Salaries and Expense / Administrative Costs	**$5,408,838**	**$5,378,502**	**-$30,336**
Direct FTE	**13,454**	**13,469**	**13,469**

[1] Excludes Superfund Research account under the jurisdiction of the Interior, Environment & Related Agencies Appropriations Subcommittee. PHS Evaluation Fund allocation to NLM also excluded.

[2] Excludes obligations from accounts (OC 25.1, 25.3 and 25.4) supporting Program Evaluations and Inter-agency Agreements related to the Research and Development Contracts mechanism.

National Institutes of Health

Detail of Full-Time Equivalent Employment (FTE)

Institutes and Centers (ICs)	FY 2013 Actual	FY 2014 Enacted	FY 2015 PB
NCI	3,103	3,103	3,103
NHLBI	942	942	942
NIDCR	253	253	253
NIDDK	630	630	630
NINDS	525	525	525
NIAID	1,977	1,977	1,977
NIGMS	183	183	183
NICHD	603	603	603
NEI	267	267	267
NIEHS	672	672	672
NIA	395	395	395
NIAMS	246	246	246
NIDCD	140	140	140
NIMH	575	575	575
NIDA	394	394	394
NIAAA	243	243	243
NINR	93	93	93
NHGRI	333	333	333
NIBIB	106	106	106
NIMHD	63	63	63
NCCAM	74	74	74
NCATS	127	127	127
FIC	62	62	62
NLM	799	799	799
OD	649	664	664
Central Services[1]	4,776	4,761	4,761
Subtotal	**18,230**	**18,230**	**18,230**
PHS Trust Fund [2]	4	4	4
CRADA (non-add) [3]	*11*	*11*	*11*
Grand Total	**18,234**	**18,234**	**18,234**

[1] Reflects FTE associated with Central Services positions whose payroll costs are covered from NIH Management Fund and NIH Service and Supply Fund resources.

[2] PHS Trust Fund positions are identified separately in Direct-funded civilian FTE category.

[3] CRADA positions are distributed across multiple ICs and are treated as non-add values.

NATIONAL INSTITUTES OF HEALTH

History of Obligations by Institute or Center[1]
Fiscal Years 2006 - 2015
(Dollars in Thousands)

Institutes and Centers	FY 2006 Actual Obligations	FY 2007 Actual Obligations	FY 2008 Actual Obligations	FY 2009 Actual Obligations	FY 2010 Actual Obligations	FY 2011 Actual Obligations	FY 2012 Actual Obligations	FY 2013 Actual Obligations	FY 2013 Comparable Budget Authority	FY 2014 Comparable Budget Authority	FY 2015 President's Budget
NCI[2]	$4,754,121	$4,792,615	$4,827,552	$4,966,927	$5,098,147	$5,058,105	5,062,763	4,789,014	$4,783,442	$4,922,771	$4,930,715
NHLBI	2,893,527	2,922,323	2,937,333	3,014,552	3,093,501	3,069,550	3,073,302	2,903,768	2,900,321	2,982,737	2,987,685
NIDCR	385,589	389,060	391,136	402,011	412,527	409,549	409,947	387,309	386,874	397,102	397,131
NIDDK[3]	1,688,511	1,702,990	1,712,188	1,761,795	1,808,905	1,792,155	1,793,706	1,694,677	1,692,748	1,741,874	1,743,336
NINDS	1,519,971	1,532,977	1,549,543	1,590,781	1,633,568	1,622,001	1,623,344	1,533,793	1,531,975	1,585,797	1,608,461
NIAID	4,274,201	4,264,034	4,286,410	4,400,398	4,515,426	4,478,595	4,482,369	4,235,094	4,230,080	4,392,670	4,423,357
NIGMS	1,916,927	1,932,481	1,942,783	1,994,426	2,048,112	2,033,663	2,425,522	2,293,044	2,290,525	2,361,894	2,368,877
NICHD	1,252,598	1,252,765	1,259,435	1,292,929	1,327,349	1,317,682	1,318,943	1,246,140	1,244,707	1,280,830	1,283,487
NEI	660,340	665,863	669,534	687,350	705,792	700,781	701,407	657,055	656,291	674,249	675,168
NIEHS[4]	630,454	647,020	651,557	668,037	694,807	683,557	684,297	646,467	645,782	664,524	665,080
NIA	1,036,559	1,045,468	1,050,998	1,079,004	1,108,208	1,100,445	1,120,391	1,040,565	1,039,399	1,169,427	1,170,880
NIAMS	502,954	507,292	510,358	523,887	538,028	534,260	534,791	505,206	504,691	519,338	520,189
NIDCD	389,623	392,937	395,515	406,516	418,001	415,104	415,500	392,540	392,113	403,493	403,933
NIMH	1,390,009	1,402,385	1,414,541	1,454,377	1,493,510	1,477,257	1,477,516	1,396,006	1,394,354	1,416,825	1,440,076
NIDA	990,405	1,001,952	1,007,295	1,039,561	1,066,909	1,050,519	1,051,410	993,404	992,232	1,015,754	1,023,268
NIAAA	431,726	435,366	437,839	449,524	461,544	458,257	458,665	433,247	432,849	445,411	446,017
NINR	136,020	137,167	137,990	141,660	145,420	144,369	144,500	136,516	136,367	140,324	140,452
NHGRI	481,339	508,240	505,380	507,210	524,131	511,469	512,258	483,650	483,107	497,128	498,451
NIBIB	293,954	296,380	299,726	307,701	316,028	313,787	337,728	319,062	318,720	326,359	328,532
NIMHD[5]	193,522	199,083	200,252	205,616	211,194	209,693	275,927	260,671	260,396	267,953	267,953
NCRR[6]	1,088,500	1,131,618	1,153,911	1,224,629	1,267,021	1,257,641	---	---	---	---	---
NCCAM	120,294	121,369	122,013	125,265	128,615	127,706	127,820	120,767	120,624	124,125	124,509
NCATS[6]	---	---	---	---	---	---	574,297	542,598	541,973	632,396	657,471
FIC	65,726	66,348	66,828	68,607	69,957	69,413	69,493	65,627	65,581	67,484	67,776
NLM[7]	311,721	321,354	323,385	329,614	340,267	336,660	364,887	316,888	352,268	367,223	372,851
ORIP & SEPA[6]	---	---	---	---	---	---	303,525	290,042	289,376	294,195	294,195
Common Fund[8]	332,556	482,961	498,240	541,133	544,028	543,017	544,930	513,461	513,476	533,039	583,039
OD - Other[9]	392,275	563,596	613,454	706,295	632,966	623,887	608,713	608,584	607,663	572,519	574,552
B&F[2]	170,456	89,114	127,227	88,815	203,056	62,161	125,308	106,676	118,109	128,663	128,663
Total, Labor/HHS Budget Authority	**$28,303,878**	**$28,804,758**	**$29,092,423**	**$29,978,620**	**$30,807,017**	**$30,401,283**	**30,623,259**	**$28,911,870**	**$28,926,041**	**$29,926,104**	**$30,126,104**
Interior/Superfund	79,101	79,111	77,531	78,070	79,201	79,045	78,928	74,864	74,871	77,349	77,349
Type I Diabetes	150,000	150,000	150,000	150,000	150,000	150,000	150,000	142,350	142,350	139,200	150,000
Total, NIH Budget Authority	**$28,532,979**	**$29,033,869**	**$29,319,954**	**$30,206,690**	**$31,036,218**	**$30,630,328**	**$30,852,187**	**$29,129,085**	**$29,143,262**	**$30,142,653**	**$30,353,453**

[1] Actual fiscal years obligations exclude all lapses and excludes NIAID Global AIDS for FY 2006 through FY 2012. FY 2013 Actual Obligations are displayed in Noncomparable and Comparable levels.

[2] NCI obligations include obligations associated with repair and improvement (R&I) related construction for the Frederick facility. Those obligations are excluded from amounts identified to B&F.

[3] Excludes amount for Type 1 Diabetes.

[4] Excludes amount allocated for Superfund Research activities from Interior, Environment & Related Agencies appropriation .

[5] NIMHD was designated as an Institute from Center starting FY 2009 under the section 10334 of the Patient Protection and Affordable Care Act (PPACA; P.L. 111-148).

[6] ICs realigned to reflect creation of NCATS.

[7] NLM is treated as a stand-alone IC starting FY 2007.

[8] Common Fund name was changed from Roadmap starting in FY 2009.

[9] Includes Bridge Award amount of $89,656 thousand for both FY 2008 and FY 2009.

NATIONAL INSTITUTES OF HEALTH
History Of Obligations By Total Mechanism *
Fiscal Years 2006 - 2015
(Dollars in Thousands)

Budget Mechanism	FY 2006 Actual Obligations	FY 2007 Actual Obligations	FY 2008 Actual Obligations	FY 2009 Actual Obligations	FY 2010 Actual Obligations	FY 2011 Actual Obligations	FY 2012 Actual Obligations	FY 2013 Actual Obligations	FY 2013 Comparable Actual Obligations [3]	FY 2014 Enacted [3]	FY 2015 President's Budget
Res. Project Grants	$15,265,348	$15,333,540	$15,688,339	$16,124,554	$16,501,300	$16,428,047	$16,550,486	$15,445,463	$15,445,463	$16,077,332	$16,196,847
Research Centers	2,659,653	2,709,259	2,946,346	3,018,710	3,082,914	3,009,480	3,040,375	$2,708,744	2,708,745	2,713,055	2,722,834
Other Research	1,624,898	1,652,501	1,779,990	1,775,387	1,794,148	1,802,937	1,808,138	$1,783,481	1,783,484	1,824,798	1,867,979
Subtotal, Res. Grants	$19,549,899	$19,695,300	$20,414,675	$20,918,651	$21,378,362	$21,240,464	$21,398,999	$19,937,688	$19,937,691	$20,615,185	$20,787,660
Research Training	731,121	763,797	770,480	776,193	775,186	771,766	761,934	$733,524	733,524	752,877	767,132
R & D Contracts	2,581,106	2,693,443	2,934,858	3,069,412	3,143,929	2,996,640	2,937,188	$2,927,077	2,895,302	2,990,346	3,030,746
Intramural Research	2,742,466	3,002,558	3,091,240	3,222,852	3,306,312	3,330,815	3,401,506	$3,247,193	3,282,734	3,395,910	3,435,324
Res. Mgt. & Support	1,098,953	1,136,197	1,372,225	1,428,138	1,509,287	1,517,630	1,530,874	$1,485,575	1,485,463	1,528,653	1,544,027
Cancer Control[1]	505,705	498,396	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Construction	29,700	14,100	0	0	0	0	0	$0	0	0	0
Library of Medicine[1]	311,721	7,376	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Office of the Director	724,831	1,046,557	523,798	616,639	632,966	623,887	609,530	$608,584	607,663	572,519	574,552
Subtotal	**$28,275,502**	**$28,857,724**	**$29,107,276**	**$30,031,885**	**$30,746,042**	**$30,481,202**	**$30,640,031**	**$28,939,641**	**$28,942,378**	**$29,855,490**	**$30,139,441**
Buildings & Facilities[2]	178,376	97,034	135,147	96,735	210,975	70,081	133,228	$114,580	126,013	136,341	136,663
Interior- Superfund	79,101	79,111	77,531	78,070	79,201	79,045	78,928	$74,864	74,871	77,349	77,349
Total, NIH Budget Authority	**$28,532,979**	**$29,033,869**	**$29,319,954**	**$30,206,690**	**$31,036,218**	**$30,630,328**	**$30,852,187**	**$29,129,085**	**$29,143,262**	**$30,142,653**	**$30,353,453**

*Obligations for actual years exclude lapse and include Type 1 Diabetes.

[1] NIH has modified its traditional budget display by mechanism so that activities of the National Cancer Institute's Cancer Prevention and Control Program and the National Library of Medicine are allocated among the various trans-NIH mechanisms of support.

[2] B&F mechanism amounts include the B&F appropriation plus dollars associated with repair and improvement (R&I) related construction for the Frederick MD facility appropriated to NCI.

[3] FY 2013 Comparable column includes all transfers and comparable adjustments. The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

National Institutes of Health
FY 2015 Congressional Justification

Programs Proposed for Elimination

The FY 2015 Budget will propose a fresh Government-wide reorganization of science, technology, engineering, and mathematics (STEM) education programs designed to enable more strategic investment in STEM education and more critical evaluation of outcomes.. As part of the reorganization four NIH STEM programs will be eliminated in FY 2015. The following table shows the programs proposed for elimination or consolidation in the FY 2015 President's Budget request.

Program	FY 2013 (Budget Authority in Millions)
NIAID Science Education Awards	$1.0
NIDA Science Education Drug Abuse Partnership Award	$0.7
NIEHS Short Term Educational Experience for Research (STEER) in the Environmental Health Sciences for Undergraduates and High School Students	$0.5
NINDS Diversity Research Education Grants in Neuroscience	$1.0

Rationale

STEM Programs (-$3.2 million):
This proposal focuses efforts around the five key areas identified by the Federal STEM Education 5-Year Strategic Plan: P-12 instruction; undergraduate education; graduate education; broadening participation in STEM to women and minorities traditionally underrepresented in these fields; and education activities that typically take place outside of the classroom.

Management Fund

General Statement

The NIH Management Fund (MF) was established on June 29, 1957, by Public Law 85-67. The MF was created to finance a variety of centralized support services and administrative activities that are required for the efficient and effective operation of all NIH programs and facilities. The services provided by the MF include a research hospital and outpatient clinic, receipt, review and referral of research and training grant applications, collaborative computer science research, police, fire, security and general administrative support services. Funds credited to the NIH Management Fund remain available for one fiscal year after the fiscal year in which they are deposited.

NATIONAL INSTITUTES OF HEALTH
Management Fund

Budget Authority by Activity
(Dollars in Thousands)

	FY 2013 Actual		FY 2014 Enacted		FY 2015 President's Budget	
	FTE	Amount	FTE	Amount	FTE	Amount
Detail						
Center for Information Technology	0	$981	0	$0	0	$0
Clinical Center	1,855	417,683	1,855	424,150	1,855	428,479
Center for Scientific Review, SREA	375	106,219	375	108,013	375	109,181
Services, OD	82	38,025	82	38,796	82	39,184
Office of Research Services, Facilities, Development & Operations	556	85,868	556	87,559	556	88,435
TOTAL	**2,868**	**$648,776**	**2,868**	**$658,519**	**2,868**	**$665,279**

NATIONAL INSTITUTES OF HEALTH
Management Fund

Budget Authority by Object Class

(Dollars in Thousands)

		FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Total compensable workyears:				
	Full-time employment	2,868	2,868	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$181	$183	$1
	Average GM/GS grade	11.7	11.7	0.0
	Average GM/GS salary	$93	$93	$0
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$77	$77	$0
	Average salary of ungraded positions	$122	$122	$0
	OBJECT CLASSES	**FY 2014 Enacted**	**FY 2015 President's Budget**	**FY 2015 +/- FY 2014**
	Personnel Compensation			
11.1	Full-Time Permanent	$146,299	$147,908	$1,609
11.3	Other Than Full-Time Permanent	85,054	85,989	936
11.5	Other Personnel Compensation	11,703	11,832	129
11.7	Military Personnel	6,391	6,455	64
11.8	Special Personnel Services Payments	4,412	4,456	44
11.9	**Subtotal Personnel Compensation**	**$253,858**	**$256,639**	**$2,782**
12.1	Civilian Personnel Benefits	$70,516	$71,221	$705
12.2	Military Personnel Benefits	4,480	4,502	22
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**328,853**	**332,363**	**3,509**
21.0	Travel & Transportation of Persons	$1,569	$1,585	$16
22.0	Transportation of Things	733	737	4
23.1	Rental Payments to GSA	1,232	1,244	12
23.2	Rental Payments to Others	8	8	0
23.3	Communications, Utilities & Misc. Charges	3,696	3,696	0
24.0	Printing & Reproduction	1,980	1,980	0
25.1	Consulting Services	$19,409	$19,409	0
25.2	Other Services	93,077	94,473	1,396
25.3	Purchase of goods and services from government	$91,146	$92,969	1,823
25.4	Operation & Maintenance of Facilities	$11,702	$11,702	0
25.5	R&D Contracts	954	954	0
25.6	Medical Care	3,927	3,927	0
25.7	Operation & Maintenance of Equipment	15,642	15,642	0
25.8	Subsistence & Support of Persons	0	0	0
	Subtotal Other Contractual Services	**$235,857**	**$239,076**	**$3,251**
26.0	Supplies & Materials	$65,720	$65,720	0
31.0	Equipment	18,863	18,863	0
32.0	Land and Structures	1	1	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	0	0	0
42.0	Insurance Claims & Indemnities	3	3	0
43.0	Interest & Dividends	4	4	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$329,666**	**$332,916**	**$0**
	Total Budget Authority by Object Class	**$658,519**	**$665,279**	**$6,760**

NATIONAL INSTITUTES OF HEALTH
Management Fund

Details of Positions

GRADE	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Total, ES Positions	5	6	6
Total, ES Salary	$864,138	$1,088,879	$1,096,760
GM/GS-15	135	140	141
GM/GS-14	263	282	287
GM/GS-13	313	336	338
GS-12	350	357	362
GS-11	484	496	497
GS-10	25	25	25
GS-9	160	167	168
GS-8	112	112	113
GS-7	199	201	202
GS-6	55	57	58
GS-5	35	37	37
GS-4	12	13	13
GS-3	6	5	5
GS-2	9	9	9
GS-1	0	0	0
Subtotal	2,158	2,237	2,255
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	1	1	1
Director Grade	12	12	13
Senior Grade	23	26	28
Full Grade	22	20	19
Senior Assistant Grade	15	14	15
Assistant Grade	8	7	7
Subtotal	81	80	83
Ungraded	844	833	821
Total permanent positions	2,138	2,220	2,228
Total positions, end of year	3,088	3,156	3,165
Total full-time equivalent (FTE) employment, end of year	2,868	2,868	2,868
Average ES salary	$172,828	$181,480	$182,793
Average GM/GS grade	11.6	11.7	11.7
Average GM/GS salary	$92,258	$93,168	$93,361

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification

Service and Supply Fund

General Statement

The NIH Service and Supply Fund (SSF) was established on July 3, 1945, under 42 U.S.C. 231. The SSF was created to finance a variety of centralized research support services and administrative activities that are required for the efficient and effective operation of all NIH programs and facilities. The SSF provides a single means for consolidating the financing and accounting of business-type operations, including the sales of services and commodities to customers. The services provided through the SSF include mainframe computing, enterprise IT software planning and development, facilities engineering, planning, and design, facility use and maintenance including leased buildings, printing, telecommunications, procurement, shipping and receiving, motor pool, research animals, fabrication and maintenance of scientific equipment, utilities and plant maintenance, finance and accounting operations, government-wide contracting for IT, biomedical engineering, security, consolidated human resources, and other administrative support services.

NATIONAL INSTITUTES OF HEALTH
Service and Supply Fund
Budget Authority by Activity
(Dollars in Thousands)

	FY 2013 Actual		FY 2014 Enacted		FY 2015 President's Budget	
	FTE	Amount	FTE	Amount	FTE	Amount
Detail						
Research Support and Administrative	883	$586,321	868	$592,184	868	$592,184
Office of Research Facilities, Development & Operations	697	458,129	697	462,710	697	462,710
Center for Information Technology	326	297,892	326	300,871	326	300,871
Clinical Center	2	195	2	197	2	197
TOTAL	**1,908**	**$1,342,537**	**1,893**	**$1,355,962**	**1,893**	**$1,355,962**

NATIONAL INSTITUTES OF HEALTH
Service and Supply Fund

Budget Authority by Object Class
(Dollars in Thousands)

		FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
Total compensable workyears:				
	Full-time employment	1,893	1,893	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$171	$171	0
	Average GM/GS grade	11.7	11.7	0
	Average GM/GS salary	$90	$90	0
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$92	$92	0
	Average salary of ungraded positions	$126	$126	0
	OBJECT CLASSES	**FY 2014 Enacted**	**FY 2015 President's Budget**	**FY 2015 +/- FY 2014**
	Personnel Compensation			
11.1	Full-Time Permanent	$176,514	$176,514	$0
11.3	Other Than Full-Time Permanent	9,805	9,805	0
11.5	Other Personnel Compensation	7,164	7,164	0
11.7	Military Personnel	2,258	2,258	0
11.8	Special Personnel Services Payments	217	217	0
11.9	**Subtotal Personnel Compensation**	**$195,958**	**$195,958**	**$0**
12.1	Civilian Personnel Benefits	$54,807	$54,807	$0
12.2	Military Personnel Benefits	1,155	1,155	0
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$251,920**	**$251,920**	**$0**
21.0	Travel & Transportation of Persons	$616	$616	$0
22.0	Transportation of Things	801	801	0
23.1	Rental Payments to GSA	67,061	67,061	0
23.2	Rental Payments to Others	97,918	97,918	0
23.3	Communications, Utilities & Misc. Charges	114,216	114,216	0
24.0	Printing & Reproduction	1	1	0
25.1	Consulting Services	$149,604	$149,604	0
25.2	Other Services	192,885	192,885	0
25.3	Purchase of goods and services from government accounts	$241,787	$241,787	0
25.4	Operation & Maintenance of Facilities	$79,539	$79,539	0
25.5	R&D Contracts	20	20	0
25.6	Medical Care	475	475	0
25.7	Operation & Maintenance of Equipment	84,928	84,928	0
25.8	Subsistence & Support of Persons	0	0	0
	Subtotal Other Contractual Services	**$1,029,851**	**$1,029,851**	**$0**
26.0	Supplies & Materials	$53,409	$53,409	0
31.0	Equipment	20,743	20,743	0
32.0	Land and Structures	23	23	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	0	0	0
42.0	Insurance Claims & Indemnities	2	2	0
43.0	Interest & Dividends	17	17	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$1,104,045**	**$1,104,045**	**$0**
	Total Budget Authority by Object Class	**$1,355,962**	**$1,355,962**	**$0**

NATIONAL INSTITUTES OF HEALTH
Service and Supply Fund

Details of Positions

GRADE	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Total, ES Positions	5	5	5
Total, ES Salary	$851,994	$853,791	$853,791
GM/GS-15	75	86	87
GM/GS-14	237	246	247
GM/GS-13	504	527	528
GS-12	301	318	318
GS-11	98	116	116
GS-10	2	4	4
GS-9	82	93	93
GS-8	38	45	45
GS-7	110	117	117
GS-6	28	29	29
GS-5	16	17	17
GS-4	16	16	16
GS-3	15	9	9
GS-2	18	10	10
GS-1	3	3	3
Subtotal	1,543	1,636	1,639
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	6	6	6
Senior Grade	4	4	4
Full Grade	5	5	5
Senior Assistant Grade	2	2	2
Assistant Grade	1	1	1
Subtotal	18	18	18
Ungraded	403	379	379
Total permanent positions	1,846	1,897	1,897
Total positions, end of year	1,968	2,035	2,038
Total full-time equivalent (FTE) employment, end of year	1,908	1,893	1,893
Average ES salary	$170,399	$170,758	$170,758
Average GM/GS grade	11.6	11.7	11.7
Average GM/GS salary	$89,318	$90,211	$90,211

FY 2015 Congressional Justification
Physicians' Comparability Allowance (PCA) Worksheet
National Institutes of Health

		CY 2013 * Actual	BY 2014** Enacted	BY 2015*** President's Budget
1) Number of Physicians Receiving PCAs		145	145	145
2) Number of Physicians with One-Year PCA		11	11	11
3) Number of Physicians with Multi-Year PCA		134	134	134
4) Average Annual PCA Physician Pay (without PCA payment)		$ 143,267	$ 144,342	$ 145,785
5) Average Annual PCA Payment		$ 23,248	$ 23,422	$ 23,657
6) Number of Physicians Receiving PCAs by Category (non-add)	Category I Clinical Position			
	Category II Research Position	144	144	144
	Category III Occupational Health			
	Category IV-A Disability Evaluation			
	Category IV-B Health and Medical Admin.	1	1	1

*FY 2013 based on actual data as of December 31, 2013.

**FY 2014 cost estimates accounts for Federal pay raises effective January 2014.

***FY 2015 cost estimates reflect anticipated January 2015 pay raise of 1%, consistent with the President's Budget request assumptions.

7) If applicable, list and explain the necessity of any additional physician categories designated by your agency (for categories other than I through IV-B). Provide the number of PCA agreements per additional category for the PY, CY and BY.

N/A

8) Provide the maximum annual PCA amount paid to each category of physician in your agency and explain the reasoning for these amounts by category.

Maximum annual PCA amount for category II and IV-B is $30,000. This amount is necessary to retain the caliber of physician needed to carry out the NIH mission which directly impacts the health of the nation.

9) Explain the recruitment and retention problem(s) for each category of physician in your agency (this should demonstrate that a current need continues to persist).(Please include any staffing data to support your explanation, such as number and duration of unfilled positions and number of accessions and separations per fiscal year.)

NIH continues to face challenges recruiting and retaining qualified physicians to the Federal service due to competition and more lucrative compensation in the private sector. The NIH consistently has a turnover rate that exceeds 10% across all the various pay plans used to compensate physicians. In FY 2013, the NIH had a 12% separation rate and a 9% accession rate for physicians. NIH physicians require unique and specialized qualifications that make it difficult to keep up with the attrition rate.

10) Explain the degree to which recruitment and retention problems were alleviated in your agency through the use of PCAs in the prior fiscal year. (Please include any staffing data to support your explanation, such as number and duration of unfilled positions and number of accessions and separations per fiscal year.)

In FY 2013, there was a total of 145 PCA recipients across NIH. In FY 2014 and beyond, a critical need will continue to exist for highly qualified, specialized physicians to support the NIH mission. With a physician turnover rate hovering at 10% the NIH requires compensation flexibilities such as PCA to attract and retain qualified physicians.

11) Provide any additional information that may be useful in planning PCA staffing levels and amounts in your agency.

N/A.

National Institutes of Health
FY 2015 Congressional Justification
Statistical Data -- Grants, Direct, and Indirect Cost Awarded
(Dollars in Thousands)

Fiscal Year	Direct Cost Awarded	Indirect Cost Awarded	Percent of Total		Percent Change	
			Direct Cost Awarded	Indirect Cost Awarded	Direct Cost Awarded	Indirect Cost Awarded
FY 2003	$14,445,631	$5,301,292	73.2%	26.8%	13.4%	11.7%
FY 2004	$14,892,783	$5,647,066	72.5%	27.5%	12.7%	9.6%
FY 2005	$15,419,089	$5,795,178	72.7%	27.3%	3.1%	6.5%
FY 2006	$15,219,138	$5,781,293	72.5%	27.5%	3.5%	2.6%
FY 2007	$15,387,745	$5,876,060	72.4%	27.6%	-1.3%	-0.2%
FY 2008	$15,295,950	$5,903,730	72.2%	27.8%	1.1%	1.6%
FY 2009	$15,683,872	$6,027,543	72.2%	27.8%	-0.6%	0.5%
FY 2010	$16,040,991	$6,193,567	72.1%	27.9%	2.5%	2.1%
FY 2011	$15,849,082	$6,173,769	72.0%	28.0%	2.3%	2.8%
FY 2012	$15,978,032	$6,182,900	72.1%	27.9%	-1.2%	-0.3%
FY 2013	$14,915,599	$5,755,617	72.2%	27.8%	-6.6%	-6.9%
FY 2014 Enacted	$15,418,424	$5,949,638	72.2%	27.8%	3.4%	3.4%
FY 2015 President's Budget	$15,553,162	$6,001,630	72.2%	27.8%	0.9%	0.9%

Note: FY 2014 and FY 2015 data represent estimates and will change as actual data is received.

Research Project Grants: Total Number of Awards and Dollars [1]
Includes Type 1, Common Fund and Bridge Awards
(Dollars in Thousands)

	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014 Enacted[2]	FY 2015 PB Request[2]
No. of Awards:										
Competing	9,129	10,323	9,714	9,121	9,386	8,706	8,986	8,234	8,997	9,326
Noncompeting	27,366	26,741	26,610	26,217	25,738	26,166	25,631	25,140	23,632	23,236
Subtotal	36,495	37,064	36,324	35,338	35,124	34,872	34,617	33,374	32,629	32,562
SBIR/STTR	1,822	1,781	1,838	1,740	1,685	1,494	1,642	1,466	1,584	1,635
Total	**38,317**	**38,845**	**38,162**	**37,078**	**36,809**	**36,366**	**36,259**	**34,840**	**34,213**	**34,197**
Average Annual Cost:										
Competing	$368.3	$367.0	$377.4	$427.2	$417.1	$427.5	$420.9	$417.7	$474.2	$443.1
Total RPGs[3]	$403.2	$404.7	$413.5	$437.5	$450.4	$452.6	$458.8	$443.7	$471.4	$475.4
Percent Change over prior year average costs:										
Competing RPGs	3.8%	-0.4%	2.8%	13.2%	-2.4%	2.5%	-1.5%	-0.8%	13.5%	-6.6%
Total RPGs[3]	0.3%	0.4%	2.2%	5.8%	2.9%	0.5%	1.4%	-3.3%	6.2%	0.8%
Average Length of Award in Years	3.8	3.8	3.8	3.8	3.8	3.7	3.5	3.5	3.5	3.5

[1] Beginning in FY 2007, RPG funded by the National Cancer Institute's Cancer Prevention & Control program and the National Library of Medicine are included in grant numbers and dollar amounts.

[2] Numbers of grants identified in FY 2014 Enacted and FY 2015 President's Budget are estimates, and will change as applications are received and selected for funding.

[3] Includes Noncompeting RPGs and Administrative Supplements and excludes SBIR/STTR.

NATIONAL INSTITUTES OF HEALTH
FY 2015 Congressional Justification
Research Project Grants Success Rates, FY 2006 - FY 2015 [1,2,3]

INSTITUTES & CENTERS	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014 Enacted	FY 2015 PB	INSTITUTES & CENTERS
NCI	19.4%	20.1%	21.0%	19.0%	17.1%	13.8%	13.6%	13.7%	13.1%	12.8%	NCI
NHLBI	19.7%	21.0%	22.0%	22.0%	19.9%	17.4%	14.7%	16.9%	18.0%	16.8%	NHLBI
NIDCR	18.6%	22.4%	20.0%	19.0%	22.2%	22.5%	21.2%	19.9%	21.3%	20.4%	NIDCR
NIDDK	21.2%	20.9%	25.0%	23.0%	25.9%	20.7%	19.8%	21.0%	23.4%	22.1%	NIDDK
NINDS	18.4%	18.7%	21.0%	21.0%	22.6%	21.1%	19.5%	19.8%	20.2%	21.2%	NINDS
NIAID	20.6%	23.0%	23.0%	19.0%	23.9%	20.2%	23.2%	18.8%	20.4%	20.9%	NIAID
NIGMS	26.0%	32.1%	27.0%	27.0%	26.9%	23.1%	24.4%	19.9%	22.0%	22.8%	NIGMS
NICHD	15.2%	20.6%	17.0%	15.0%	15.2%	12.4%	12.5%	10.8%	11.5%	10.2%	NICHD
NEI	23.4%	26.6%	30.0%	30.0%	26.9%	28.8%	29.8%	23.7%	24.9%	22.1%	NEI
NIEHS	22.3%	18.5%	18.0%	18.0%	25.1%	14.7%	14.3%	15.3%	14.1%	13.2%	NIEHS
NIA	17.4%	22.1%	20.0%	18.0%	14.5%	16.1%	15.5%	13.6%	18.5%	16.7%	NIA
NIAMS	19.3%	20.0%	21.0%	20.0%	21.4%	14.9%	15.6%	15.9%	16.9%	17.5%	NIAMS
NIDCD	28.4%	31.0%	29.0%	32.0%	30.2%	27.5%	26.6%	22.5%	24.3%	24.0%	NIDCD
NIMH	19.7%	22.1%	21.0%	22.0%	22.1%	17.1%	21.6%	18.7%	18.9%	22.7%	NIMH
NIDA	19.8%	23.4%	24.0%	22.0%	19.8%	18.2%	21.2%	19.5%	16.3%	21.6%	NIDA
NIAAA	27.1%	27.2%	26.0%	24.0%	26.5%	18.6%	18.4%	19.5%	19.5%	19.5%	NIAAA
NINR	17.6%	25.6%	20.0%	21.0%	13.2%	8.5%	13.0%	9.1%	9.0%	8.0%	NINR
NHGRI	33.5%	28.0%	32.0%	34.0%	33.6%	27.4%	23.9%	20.5%	15.2%	14.0%	NHGRI
NIBIB	16.9%	21.5%	19.0%	18.0%	16.0%	12.9%	12.1%	13.7%	12.4%	16.5%	NIBIB
NIMHD[3]	N/A	N/A	N/A	11.0%	8.0%	11.9%	9.9%	4.3%	10.3%	4.5%	NIMHD
NCCAM	13.5%	10.8%	12.0%	12.0%	11.0%	9.1%	9.5%	11.6%	8.5%	10.9%	NCCAM
NCATS[4]	N/A	N/A	N/A	N/A	N/A	N/A	0.0%	0.0%	20.0%	20.0%	NCATS
FIC	19.3%	25.1%	28.0%	21.0%	26.1%	11.9%	16.0%	14.6%	53.8%	22.4%	FIC
NLM[5]	N/A	18.7%	21.0%	12.0%	21.1%	16.1%	12.8%	12.3%	16.1%	12.9%	NLM
ORIP & SEPA[6,7]	13.2%	20.3%	15.0%	22.0%	22.0%	21.3%	18.6%	20.0%	12.3%	11.3%	ORIP & SEPA
Common Fund	10.1%	7.0%	12.0%	17.0%	11.1%	11.3%	8.0%	9.2%	7.3%	7.5%	Common Fund
NIH[8]	**20.0%**	**21.3%**	**21.0%**	**21.0%**	**20.5%**	**17.5%**	**17.5%**	**16.7%**	**17.3%**	**17.4%**	**NIH**

[1] Includes Special type 1Diabetes administered by NIDDK. Excludes NIEHS Superfund Research account administered by NIEHS.

[2] Application success rates represent the percentage of applications that are awarded during the fiscal year.

[3] Success Rates identified in FY 2014 and FY 2015 are estimates, and will change as applications are received and selected for funding.

[4] NIMHD (formally NCMHD) success rates are not available due to co-funding agreements with other ICs through FY 2008. NIMHD only co-funded competing RPGs with other ICs until FY 2009.

[5] The National Center for Advancing Translational Sciences (NCATS) was established concurrent with the dissolution of National Center for Research Resources (NCRR) effective FY 2012.

[6] NLM success rate is displayed for FY 2007 and forward due to change in the reporting requirements. As of FY 2007, NLM funding is no longer reflected as an individual line item on the NIH Budget Mechanism Table.

[7] Success rate data associated with grants funded from the OD appropriation unrelated to the Common Fund or ORIP & SEPA is not included. Collection of this information was initiated in FY 2012.

[8] SEPA program was proposed for termination in FY 2014 as part of a government-wide initiative to reconfigure Science, Technology, Engineering, and Mathematics (STEM) activities.

[9] NIH success rate exludes application and grant data from OD Non-Common Fund and OD Non-ORIP & SEPA accounts.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Common Fund (CF)

NATIONAL INSTITUTES OF HEALTH
Common Fund
Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2013 Actual		FY 2014 Enacted[2]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	299	$139,519	296	$138,125	343	$160,280	47	$22,155
Administrative Supplements	*(63)*	13,977	*(90)*	20,064	*(91)*	20,064	*(1)*	0
Competing:								
Renewal	0	0	0	0	0	0		
New	132	149,160	140	158,488	150	169,297	10	10,809
Supplements	0	0	0	0	0	0		
Subtotal, Competing	132	$149,160	140	$158,488	150	$169,297	10	$10,809
Subtotal, RPGs	431	$302,656	436	$316,677	493	$349,641	57	$32,964
SBIR/STTR	0	0	0	0	0	0		
Research Project Grants	431	$302,656	436	$316,677	493	$349,641	57	$32,964
Research Centers:								
Specialized/Comprehensive	56	$79,374	60	$85,201	79	$112,658	19	$27,457
Clinical Research	0	0	0	0	0	0		0
Biotechnology	1	2,964	1	2,964	1	2,964		0
Comparative Medicine	3	6,062	3	6,062	3	6,249		187
Research Centers in Minority Institutions	0	0	0	0	0	0		0
Research Centers	60	$88,399	64	$94,227	83	$121,871	19	$27,644
Other Research:								
Research Careers	10	$1,305	22	$2,822	26	$3,322	4	$500
Cancer Education	0	0	0	0	0	0		0
Cooperative Clinical Research	0	0	0	0	0	0		0
Biomedical Research Support	0	0	0	0	0	0		0
Minority Biomedical Research Support	0	0	0	0	0	0		0
Other	38	31,989	44	37,025	72	60,317	28	23,292
Other Research	48	$33,294	66	$39,847	98	$63,639	32	$23,792
Total Research Grants	539	$424,349	566	$450,751	674	$535,151	108	$84,400
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0		$0
Institutional Awards	0	0	0	0	0	0		0
Total Research Training	0	$0	0	$0	0	$0		$0
Research & Develop. Contracts	0	$45,784	0	$45,784	0	$12,903		-$32,881
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*		*$0*
Intramural Research	0	30,718	0	20,316	0	20,519		203
Res. Management & Support	0	12,624	0	14,323	0	14,466		143
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*		*0*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	0	$513,476	0	$533,039	0	$583,039		$50,000

[1] All items in italics and brackets are non-add entries. FY 2013 and FY 2014 levels are shown on a comparable basis to FY 2015.

[2] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

Major Changes in the Fiscal Year 2015 President's Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanisms and activity detail and these highlights will not sum to the total change for the FY 2015 President's Budget for the Common Fund, which is $50.000 million more than the FY 2014 Enacted level, for a total of $583.039 million.

Research Project Grants (+$32.964 million: total $349.641 million):
The NIH Common Fund expects to support a total of 493 Research Project Grant (RPG) awards in FY 2015. Noncompeting RPGs will increase by 47 awards and $22.155 million. New RPGs will be awarded in Common Fund programs to be launched in FY 2015 as well as in new initiatives within ongoing Common Fund programs.

Research Centers (+$27.644 million: total $121.871 million):
The NIH Common Fund plans to support a total of 83 Research Center Awards in FY 2015. The launch of NIH-initiated Centers of Excellence in Biomedical Big Data within the Big Data to Knowledge (BD2K) program accounts for most of the increase in funding.

Other Research (+$23.792 million: total $63.639 million):
The estimated increase in Common Fund support for the Other Research mechanism includes a request to use $30.000 million in Other Transaction Authority (OTA). OTA funds will be used to support programs and activities that aim to achieve rapid technology development. One anticipated use for OTA funds in FY 2015 is a new program under consideration, Bioelectronic Medicines, a DARPA-like program that is a high risk, goal-driven endeavor.

Research and Development Contracts (-$32.881 million: total $12.903 million):
The estimated decrease in Research and Development Contracts reflects a planned completion of tissue procurement activities supported via contracts within the Genotype-Tissue Expression (GTEx) program. In FY 2015, GTEx will shift focus to concentrate on data generation and analysis made possible through tissues procured by these contracts.

NATIONAL INSTITUTES OF HEALTH
Common Fund by Initiative
(Dollars in Thousands)

Title of Initiative	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
High-Risk Research			
NIH Director's Pioneer Award	32,722	27,906	21,158
NIH Director's New Innovator Award Program	86,638	91,301	80,300
Transformative R01's	78,352	61,650	53,915
NIH Director's Early Independence Award Program	12,421	16,747	20,388
Subtotal, High-Risk Research	210,133	197,604	175,761
Big Data to Knowledge (BD2K)			
Big Data to Knowledge (BD2K)	704	18,727	49,832
Enhancing the Diversity of the NIH-Funded Workforce			
BUILD Initiative	3,086	27,818	35,150
National Research Mentoring Network (NRMN)	880	2,731	2,375
Coordination and Evaluation Center (CEC)	96	1,958	1,900
Subtotal, Enhancing the Diversity of the NIH-Funded Workforce	4,062	32,507	39,425
Epigenomics			
Mapping Centers	335	2,172	0
Human Health and Disease	3,458	3,008	3,000
Data Management Center for the Mapping Centers	2,998	0	0
Technology Development in Epigenetics	3,494	3,870	0
Pharmacology	3,750	4,051	4,000
Subtotal, Epigenomics	14,035	13,101	7,000
Extracellular RNA Communication			
Data Management and Resource/Repository (DMRR)	2,595	2,722	2,438
Reference Profiles of Human Extracellular RNA	80	4,075	4,078
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	7,220	7,443	7,233
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	7,831	8,808	14,132
Subtotal, Extracellular RNA Communication	17,726	23,048	27,881
Genotype-Tissue Expression (GTEx) Resources			
Genotype-Tissue Expression (GTEx) Resources	31,872	51,973	9,649
Health Care Systems Research Collaboratory			
NIH-HMORN Coordinating Center	2,694	2,505	1,733
Expansion Activities	0	9,760	10,755
Subtotal, Health Care Systems Research Collaboratory	2,694	12,265	12,488
Illuminating the Druggable Genome			
Knowledge Management Network	0	3,096	3,091
Technology Development	0	2,604	2,609
Subtotal, Illuminating the Druggable Genome	0	5,700	5,700
Strengthening the Biomedical Research Workforce			
Director's Workforce Innovation Award to Enhance Biomedical Research Training	3,727	6,750	6,750
Undiagnosed Disease Program			
Undiagnosed Diseases Program Network	10,341	18,770	28,800
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	300	980	900
Subtotal, Undiagnosed Disease Program	10,641	19,750	29,700

NATIONAL INSTITUTES OF HEALTH
Common Fund by Initiative
(Dollars in Thousands)

Title of Initiative	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Building Blocks, Biological Pathways and Networks			
National Technology Centers for Networks and Pathways (TCNPs)	9,762	110	0
Bioinformatics and Computational Biology			
National Centers for Biomedical Computing	3,436	0	0
Re-engineering the Clinical Research Enterprise			
Translational Research Core Services	4,972	0	0
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	4,143	319	0
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and CRTP and MSTP Expansions	1,066	1,100	0
Subtotal, Re-engineering the Clinical Research Enterprise	10,181	1,419	0
Library of Integrated Network-Based Cellular Signatures (LINCS)			
Perturbation-Induced Data and Signature Generation Centers (U54)	5,303	10,000	10,000
New laboratory-based technology development	2,686	0	0
Computational Tool Development and Integrative Data Analysis	1,686	0	0
Data Integration	15	0	0
Subtotal, Library of Integrated Network-Based Cellular Signatures (LINCS)	9,690	10,000	10,000
Gulf Long-term Follow-up of Workers Study			
Gulf Long-term Follow-up of Workers Study	5,459	2,500	0
Global Health			
Medical Education Partnership Initiative (MEPI)	2,910	3,000	0
Human Heredity and Health in Africa (H3Africa)	6,710	9,302	9,102
Subtotal, Global Health	9,620	12,302	9,102
Health Economics			
Changing Incentives for Consumers, Insurers, and Providers	1,319	625	665
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	2,783	3,943	4,395
Economics of Prevention	3,689	3,648	3,197
Data Infrastructure to Enable Research on Health Reform	1,723	495	77
Subtotal, Health Economics	9,514	8,711	8,334
Human Microbiome			
Sequence a Reference Set of Genomes	0	1,958	0
Demonstration Projects	742	0	0
Evaluation of multi-'omic data in understanding the microbiome's role in health and disease	5,403	6,892	5,000
Subtotal, Human Microbiome	6,145	8,850	5,000
NIH Center for Regenerative Medicine (NCRM)			
NIH Center for Regenerative Medicine (NCRM)	2,351	1,210	1,000
Good Manufacturing Process (GMP)	250	250	250
Cell Therapy Projects	0	4,040	4,250
Cell-Based Screenings	0	2,500	2,500
Subtotal, NIH Center for Regenerative Medicine (NCRM)	2,601	8,000	8,000

NATIONAL INSTITUTES OF HEALTH
Common Fund by Initiative
(Dollars in Thousands)

Title of Initiative	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget
Metabolomics			
Comprehensive Metabolomics Research Cores	12,822	12,796	10,935
Interdisciplinary Training in Metabolomics	4,322	3,553	3,554
Metabolomics Technology Development	2,381	2,513	2,502
Metabolomics Reference Standards Synthesis	1,263	1,880	1,960
Metabolomics Data Sharing and Program Coordination Core	964	2,489	1,913
Subtotal, Metabolomics	21,752	23,231	20,864
Molecular Libraries and Imaging			
Creation of NIH Bioactive Small Molecule Library & Screening Centers	46,029	574	0
Cheminformatics	243	0	0
Technology Development	121	0	0
Subtotal, Molecular Libraries and Imaging	46,393	574	0
Knockout Mouse Phenotyping Program			
Production, Characterization, and Cryopreservation	6,264	9,711	6,449
Phenotyping and Data Release	7,814	6,501	6,701
Data Coordination	657	488	550
Subtotal, Knockout Mouse Phenotyping Program	14,735	16,700	13,700
Nanomedicine			
Nanomedicine Development Centers	12,000	12,000	0
Protein Capture			
Antigen Production	49	900	0
Production of anti-TF antibodies	4,144	4,054	4,875
New Reagent Technology Development and Piloting	4,842	6,046	6,125
Subtotal, Protein Capture	9,035	11,000	11,000
Regulatory Science			
Advancing Regulatory Science through novel research and science-based technologies	24	0	0
Microphysiological Systems for Drug Efficacy and Toxicity Testing	6,010	5,300	4,000
Drug Repurposing	12,878	0	0
Subtotal, Regulatory Science	18,912	5,300	4,000
Structural Biology			
Membrane Protein Production	7,792	368	0
Single Cell Analysis			
Pilot Studies to Evaluate Cellular Heterogeneity	5,439	7,797	5,882
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	3,073	4,505	4,550
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	5,619	7,998	7,716
Single Cell Analysis Challenges	60	1,061	1,100
Subtotal, Single Cell Analysis	14,191	21,361	19,248
Science of Behavior Change			
Mechanisms of Change	4,233	3,775	0
Strategic Planning Funds	2,431	5,413	2,611
Subtotal Common Fund	513,476	533,039	476,045
New Initiatives in Common Fund	0	0	106,994
Total Common Fund	513,476	533,039	583,039

Justification of Budget Request

Common Fund

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as Amended.

Budget Authority (BA):

	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 + /- FY 2014
BA	$513,475,595	$533,039,000	$583,039,000	$50,000,000
FTE	0	0	0	0

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Director's Overview

The NIH Common Fund supports research in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserve special emphasis and would benefit from strategic coordination and planning across the NIH Institutes and Centers (ICs). To this end, Common Fund programs tackle major challenges in biomedical research that affect many diseases or conditions or that broadly relate to human health. Collectively, Common Fund programs address challenges and opportunities that have been identified as being the highest priority for the scientific research community and the NIH. Many Common Fund programs support the NIH Director's priority themes for FY 2015:

1. Today's Basic Science for Tomorrow's Breakthroughs
2. Precision Medicine
3. Big Opportunities in Big Data
4. Nurturing Talent and Innovation

Additionally, the Common Fund's High-Risk High-Reward program supports four unique awards for exceptionally creative and innovative scientists at various career stages who propose highly innovative approaches to tackle the most pressing contemporary challenges in biomedical research.

Program Portrait: High-Risk High-Reward Research

FY 2014 Level: $197.6 million
FY 2015 Level: $175.8 million
Change: -$21.8 million

Research that aims to transform science is inherently difficult; if it was either obvious or easy, the need for transformation would not exist. Although all of the Common Fund programs encourage risk-taking to overcome significant challenges in research, most of them involve designated funds for particular high risk objectives or approaches. However, the High-Risk High-Reward program (http://commonfund.nih.gov/highrisk/index.aspx) supports four complementary initiatives that support exceptionally creative scientists proposing innovative and transformative research in a scientific area of their choosing. These initiatives include the Pioneer Awards, New Innovator Awards, Transformative Research Awards, and Early Independence Awards.

Since the CF HRHR program tests new ways of supporting innovation, the NIH commissioned a rigorous external evaluation of the most mature of these initiatives, the Pioneer Awards. Comparison of research from Pioneer Awards, R01s, and research funded by the Howard Hughes Medical Institute (HHMI) showed that the Pioneer program has been successful in attracting and supporting research that is more innovative and has greater impact than R01s, and it is comparable to HHMI-supported research. Based on the success of the High-Risk High-Reward program, ICs have embraced these funding mechanisms and have committed to their support. While the CF will provide the first year of support for new Pioneer and Transformative Research Awards, ICs will support outyear costs. The CF will continue to fully support New Innovator and Early Independence Awards. Through a combination of CF and IC support, the overall NIH investment in these initiatives is steady, demonstrating NIH's commitment to nurturing scientific talent and innovation.

Overall Budget Policy:
The FY 2015 President's Budget Request for the Common Fund is $583.039 million, an increase of $50.000 million, or 9.4 percent above the FY 2014 Enacted level. The Common Fund will continue to support high priority research with trans-NIH relevance in FY 2015. As mature programs transition out of the Common Fund, new programs are being established through strategic planning activities that identify potentially transformative areas of research where limited-term Common Fund investment can have a catalytic impact.

Selected Program Narratives

The Common Fund supports more than 25 programs, most of which consist of a series of integrated initiatives that collectively address a set of goals that aim to transform the way research is conducted, the way that health and disease are understood, and/or the way that diseases are diagnosed or treated. These programs span a wide range of biomedical research fields and encompass both basic and translational research. We highlight here programs that exemplify the science supported.

Big Data to Knowledge (BD2K)

As biomedical tools and technologies rapidly improve, researchers are producing and analyzing an ever-expanding amount of complex biological data called "Big Data." As one component of an NIH-wide strategy, the Common Fund, in concert with the NIH Institutes and Centers, is supporting the Big Data to Knowledge (BD2K) program (http://commonfund.nih.gov/bd2k/),

which aims to facilitate broad use of biomedical big data, develop and disseminate analysis methods and software, enhance training in the science of big data, and establish a network of collaborating centers of excellence. Begun as a planning phase in FY 2013 and ramped up in FY 2014, the BD2K program will undergo further expansion in FY 2015 with the planned support of a data catalogue, frameworks for the development of community-based standards, software development, and establishment of NIH-initiated Centers of Excellence for biomedical big data.

Budget Policy:
The FY 2015 President's Budget estimate is $49.832 million for the BD2K program, an increase of $31.105 million or 166.1 percent above the FY 2014 Enacted level. This estimated increase in funding will be used to support activities described above.

Enhancing the Diversity of the NIH-Funded Workforce

The Enhancing the Diversity of the NIH-Funded Workforce program (http://commonfund.nih.gov/diversity/) aims to develop and test innovative approaches to biomedical research training and mentoring. The impetus for the program is the recognition that current efforts in this arena over the past two decades have not resulted in significant change at a population level: individuals from racial and ethnic minorities, from economically disadvantaged backgrounds, and those with disabilities remain underrepresented in biomedical research. Although these individuals enter college and express an interest in science at the same rate as majority students, they do not persist in science training at the same rate. Social science research has tested interventions on a small scale that could alter this trend; the Common Fund program will provide funds to test these ideas and other innovative approaches on a large scale to determine what works and for whom. This program consists of three highly integrated initiatives: a National Research Mentoring Network (NRMN), which will develop and implement novel mentoring strategies nationwide; the Building Infrastructure Leading to Diversity (BUILD) initiative, which will develop novel training approaches, including the support of training infrastructure and faculty support; and the Coordination and Evaluation Center (CEC), which will bring the whole consortium together and develop methods of evaluating each new approach. The program was launched with six-month planning grants in FY 2013 for BUILD and the NRMN. Five year awards will be issued in FY 2014 for BUILD, NRMN, and the CEC. Awardee institutions, in partnership with the NIH, will develop and test hypotheses about how to best prepare people from diverse backgrounds for research careers, with the expectation that transformative models for training and mentoring will be developed and trainees will advance to successful careers in biomedical research. Proven approaches will be broadly disseminated to provide maximum impact for diverse trainees across the country. In FY 2015, the BUILD initiative will expand to incorporate additional trainees.

Program Portrait: Building Infrastructure Leading to Diversity (BUILD) initiative: one component of the Enhancing the Diversity of the NIH-Funded Research Workforce program

FY 2014 Level: $27.8 million
FY 2015 Level: $35.2 million
Change: + $7.4 million

Although several training programs have been developed which aim to support diverse student groups, BUILD is unique in its partnership with the CEC and NRMN. Several innovative training strategies will be tested through BUILD, but exposure to meaningful research experiences is expected to be a common component of these awards. Student exposure to research at the undergraduate stage is one variable associated with improved academic performance and sustained interest in research careers in the basic and biomedical sciences. The Building Infrastructure Leading to Diversity (BUILD) initiative, one of three initiatives within the Enhancing the Diversity of the NIH-Funded Workforce program, will therefore emphasize research opportunities for students as one effective way to motivate students from diverse backgrounds to enter into and persist in biomedical research career paths . However, even within this aspect of BUILD awards, important questions of efficacy will be addressed to determine optimal practices for provision of scholarships, lab training methods, etc. To add to this approach, BUILD awardee institutions will develop additional highly creative and innovative methods to engage students in research, including those highly talented individuals who might otherwise not elect research careers. Flexibility to innovate is a hallmark of the BUILD initiative, and institutions are expected to develop transformative approaches that leverage and move beyond existing programs and paradigms. The CEC will monitor success of these approaches in real time, and adjustments will be made throughout the life of the awards to optimize success. Successful approaches are ultimately expected to supplant less effective practices and methods to have a broad and sustained impact.

The BUILD Primary (applicant) Institution eligibility criteria are intended to target funds to relatively under-resourced institutions (less than $7.5 million in annual NIH research project grant funding) with a demonstrated commitment to students from financially disadvantaged backgrounds (at least 25 percent of students must be Pell grant recipients). These institutions typically emphasize undergraduate training and may be ideally poised to encourage students from diverse backgrounds to enter research careers. BUILD Primary Institutions are encouraged to form partnerships to broaden the potential pool of participating students and maximize opportunities for research training and faculty and staff development. Potential partners include Graduate/Medical Partners (medical and graduate institutions that do not have undergraduate programs but do engage in research activities and that receive less than $7.5 million annually in NIH research project grant funding), Pipeline Partners (two- or four-year undergraduate institutions that will expand the pool of students engaged in BUILD activities), and Research Partners (research-intensive institutions). Motivation for all partner institutions to participate is expected to be the recognition that diversity – in background, race, ethnicity, physical ability, disciplinary thought, etc. – drives innovation and that this is required for scientific progress.

Budget Policy:
The FY 2015 President's Budget estimate is $39.425 million for the Enhancing the Diversity of the NIH-Funded Workforce program from the Common Fund, an increase of $6.918 million, or 21.3 percent above the FY 2014 Enacted level. The estimated increase in funding will be used to support additional trainees within the BUILD initiative.

Epigenomics

The Common Fund's Epigenomics program (http://commonfund.nih.gov/epigenomics/) is developing resources, tools, and technologies to enable investigations of the role of epigenomic modifications (modifications to DNA that do not change gene sequence, but can alter gene expression) in human health and disease. The Epigenomics program has almost 90 reference

maps of epigenomic modifications in healthy human cells and tissues, as well as numerous resources and tools that are being disseminated to and used by the biomedical research community. Researchers in the Epigenomics program have published landmark studies on the role of epigenomic modifications in normal development and disease, including recent papers that reveal important insights about the role of epigenomic changes during development as stem cells differentiate into specific cell types, such as heart, brain, and skin. In FY 2013, the Epigenomics program launched a Functional Epigenomics initiative, which aims to develop novel tools and technologies to enable manipulation of the epigenome in a tissue, cell, or gene-specific fashion, and/or with temporal control. Such tools and technologies are needed for precise manipulation of the epigenome in order to discover fundamental biological principles, as well as develop novel epigenomic therapeutics. In FY 2015, the Epigenomics program undergoes a planned decrease due to the completion of the Technology Development in Epigenetics initiative.

Budget Policy:
The FY 2015 President's Budget estimate is $7.000 million for the Epigenomics program, a decrease of $6.101 million, or 46.6 percent below the FY 2014 Enacted level. This decrease reflects the planned completion of the Technology Development in Epigenetics initiative and the Epigenomics Mapping Centers.

Extracellular RNA Communication

Ribonucleic acid (RNA) was once thought to exist in a stable form only inside cells, where it served as an intermediate in the translation of proteins from genes. However, recent research indicates that RNAs can play a role in a variety of complex functions, including newly discovered mechanisms of cell-to-cell communication via RNAs that are exported from the cell. The impact of these extracellular RNAs, or exRNAs, is currently unknown. The Common Fund's Extracellular RNA Communication program (http://commonfund.nih.gov/exrna/) aims to capitalize on the opportunity to understand entirely new paradigms of information exchange based on the release, transport, uptake, and regulatory role of exRNAs. The Extracellular RNA Communication program is supporting awards with the following aims: 1) to determine the biological principles that guide exRNA generation, secretion, uptake, and function; 2) to develop a catalogue of exRNAs found in healthy human body fluids; 3) to identify exRNA biomarkers that can be used to diagnose and monitor disease progression and response to therapy; 4) to develop and demonstrate the potential for clinical utility of exRNAs as therapeutic agents; and 5) to develop a community-wide resource for exRNA standards, protocols, and data. In FY 2015, awards in the Clinical Utility of exRNAs for Biomarker and Therapy Development initiatives will expand from pilot studies to pre-clinical qualification and validation studies.

Budget Policy:
The FY 2015 President's Budget estimate is $27.881 million for the Extracellular RNA Communications program, an increase of $4.833 million, or 21.0 percent above the FY 2014 Enacted level. The estimated increase in funding will be used to support expansion of successful pilot studies using exRNAs as biomarkers or therapeutics to pre-clinical studies.

Genotype-Tissue Expression (GTEx)

Some diseases result from sequence variation within the protein-coding region of specific genes; however, many diseases involve changes in DNA that lie outside of any gene coding region, making it difficult to determine how the change leads to disease. The Genotype-Tissue Expression (GTEx) program (http://commonfund.nih.gov/GTEx/) provides data on how human DNA variation correlates with variation in gene expression levels, which is often caused by changes in DNA that lie outside of the gene coding region. These data will strengthen the power of genome-wide association studies to identify potential new gene targets for therapies. Initiated in FY 2010 as a two-year pilot, and having met the milestones of the pilot phase, GTEx underwent an expansion in FY 2013 to build a comprehensive data and sample resource of genetic variation and gene expression profiles in multiple human tissues. The GTEx program has been highly successful in procuring samples, extracting high quality RNA from tissues, and obtaining data from gene expression array and RNA sequencing experiments. Additionally, a number of Standard Operating Procedures and best practices for specimen collection are in place and available for use by the biomedical research community. Data and biospecimens are being made available to the research community to support additional molecular analyses of GTEx samples that will add scientific value to the resource as a whole. In FY 2015, tissue procurement efforts will wind down, as the GTEx program focuses on data generation and analysis.

Budget Policy:
The FY 2015 President's Budget estimate is $9.649 million for the GTEx program, a decrease of $42.324 million, or 81.4 percent below the FY 2014 Enacted level. The estimated decrease reflects the planned reduction in tissue procurement activities.

Health Care Systems (HCS) Research Collaboratory

The Health Care Systems (HCS) Research Collaboratory program (http://commonfund.nih.gov/hcscollaboratory/) aims to strengthen the national capacity to implement cost-effective large-scale research studies that engage health care delivery organizations as research partners. This program will provide a framework of implementation methods and best practices that will enable the participation of many health care systems in clinical research. These methods and practices are being tested and honed within the context of pragmatic clinical trials, which measure the effectiveness of treatments in real world settings. A Coordinating Center serves as the central resource for the development of guidelines and best practices for the effective conduct of research studies in partnership with health care systems. The HCS Research Collaboratory also supports efficient, large-scale pragmatic clinical trials focused on the management of patients with multiple chronic health conditions. The pragmatic trials must address questions of major public health impact and test interventions that can be applied broadly to the patient population and are suitable for use in many health systems, with the broad goal of determining whether the interventions improve health outcomes of patients with multiple chronic conditions.

Budget Policy:
The FY 2015 President's Budget estimate is $12.488 million for the HCS Research Collaboratory program, an increase of $0.223 million, or 1.8 percent above the FY 2014 Enacted level. This level of funding reflects the planned decrease in support for the coordinating center, and an increase in support to allow expansion of successful pragmatic clinical trials for multiple chronic conditions from a planning phase to an implementation phase.

Illuminating the Druggable Genome (New in FY 2014)

The Illuminating the Druggable Genome (IDG) program (http://commonfund.nih.gov/IDG/) aims to increase our understanding of the properties and functions of poorly understood proteins within four of the most commonly drug-targeted protein families: the G-protein coupled receptors (GPCRs), nuclear receptors (NRs), ion channels, and protein kinases. This program is expected to catalyze discovery of truly novel biology and identify proteins as candidates for further exploration as targets for therapeutic development. The IDG program will support the adaptation and development of scalable technologies to enable exploration of large numbers of proteins within the four protein classes that represent the druggable genome, using medium- to high-throughput approaches rather than repeating the "one at a time" approach that might otherwise be undertaken. A Knowledge Management Center will be established to develop an integrated informatics solution that encompasses data accrual, analysis, data-driven prioritizations, and abstraction that will help identify gaps in knowledge of these proteins, as well as a web portal to promote efficient and user-friendly query and browsing tools that will bring together information from multiple data sources.

Budget Policy:
The FY 2015 President's Budget estimate is $5.700 million for the Illuminating the Druggable Genome program, no change from the FY 2014 Enacted level. The estimated funding level reflects ongoing support for the Knowledge Management Center and technology development.

Strengthening the Biomedical Research Workforce

The Strengthening the Biomedical Research Workforce program (http://commonfund.nih.gov/workforce/) aims to enhance training opportunities for early career scientists to prepare them for a variety of career options in the dynamic biomedical research workforce landscape. This program is supporting the Broadening Experiences in Scientific Training (BEST) awards to develop innovative approaches to complement traditional research training in biomedical sciences. Awardee institutions are collaborating with non-academic partners to ensure that experts from a broad spectrum of research and research-related careers contribute to coursework, rotations, internships, and other forms of exposure for trainees. Awardee institutions are working together to define needs and share best practices so that proven approaches can be broadly disseminated and adopted by the biomedical research training community. This program is expanding in FY 2014 to accommodate a second group of institutions; support for these awards will continue in FY 2015.

Budget Policy: The FY 2015 President's Budget estimate is $6.750 million for the Strengthening the Biomedical Research Workforce program, no change from the FY 2014 Enacted level. The estimated funding level reflects ongoing support for two cohorts of BEST awardees.

Undiagnosed Diseases Network

It is estimated that rare diseases affect 25 to 30 million Americans. Often times, because their diseases are so uncommon or have never been described before, these individuals go for long periods of time without a diagnosis, as do those with rare variants of common diseases. To aid in the diagnosis of rare and new diseases, the Common Fund's Undiagnosed Diseases Network (UDN) (http://commonfund.nih.gov/diseases/) is establishing clinical sites at academic centers across the country. The UDN builds upon the experience and expertise of the NIH intramural Undiagnosed Diseases Program, established in 2008, and its cross-disciplinary approach to diagnosing both rare and new diseases. This Network will catalyze the field of rare disease research by bringing state of the art medical and genomic approaches to bear on a myriad of diseases, bringing together basic and clinical researchers to elucidate underlying biological mechanisms to identify treatments and training the next generation of clinical researchers to use these approaches in disease diagnosis. The insights gained from understanding rare diseases may provide important clues about the pathology and potential treatments of a host of common diseases as well. Furthermore, through the support of mechanistic studies, the Network hopes to aid in disease management strategies for patients. In FY 2015, the Network clinical sites and coordinating center will expand as the Network begins to increase patient recruitment.

Budget Policy:
The FY 2015 President's Budget estimate is $29.700 million for the Undiagnosed Diseases Network, an increase of $9.950 million, or 50.4 percent above the FY 2014 Enacted level. The increased level of funding will support expansion of Network clinical sites, core laboratories, and the coordinating center as this program increases patient recruitment.

Strategic Planning and Evaluation

The Common Fund's ten year restriction on support for any given program is designed to create a churn of funds so that new challenges and opportunities may be addressed each year. Strategic Planning is therefore a critical activity for the Common Fund. Conducted annually, the Strategic Planning process allows the NIH to be nimble and adaptive to the changing scientific landscape. This process is a collaborative activity between the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)/Office of Strategic Coordination (OSC) and the ICs. Common Fund strategic planning encompasses both the identification of broadly relevant scientific challenges and opportunities for strategic investments using the Common Fund (Phase 1 planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic identified in Phase 1 (Phase 2 planning). Phase 1 strategic planning involves gathering broad input from external stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase 2 strategic planning involves more specific consultations with external experts, analysis of

the NIH and worldwide portfolios of research on the given topic, and literature reviews to articulate specific gaps and areas of research where opportunities for transformative progress are possible.

Since Common Fund programs are goal driven, evaluation is critical and increasingly important as more programs near the end of their support period. Evaluation is also conducted as a partnership between DPCPSI/OSC and the ICs, and it includes both formal and informal evaluative activities. Informal evaluation involves convening grantees and NIH-wide teams to review progress, discuss new challenges, and develop strategies to adapt as part of routine program management. It also involves gathering input from external consultants and using their input, together with internal analysis, to help guide the implementation of the program. Formal evaluations involve the development of baseline data for new programs and the development of multiple metrics of outcomes. Utility of data, resources, technologies, etc are assessed through surveys and the analysis of bibliometric data.

Budget Policy:
The FY 2015 President's Budget estimate is $2.611 million, a decrease of $2.802 million, or 51.8 percent below the FY 2014 Enacted level. The funds will be used to implement a strategic planning process to identify areas of scientific opportunity that are ripe for short-term, catalytic support from the Common Fund. Funds will also be used to evaluate the outputs and outcomes of both ongoing and mature programs.

Funds Available for New Programs

As mature initiatives end or transition out of the Common Fund, funds are available to address new challenges. The strategic planning process described above has produced new potential program areas where Common Fund investment could have a broad, transformative impact. New programs for FY 2015 may address: 3D Nucleome, Bioelectronic Medicines, Citizen Science, Glycomics, and/or Mechanisms Underlying Benefits from Physical Activity. These programs may change in nature or scope depending on scientific opportunities and/or available funding.

- 3D Nucleome: To study nuclear architecture and its relationship to gene expression and cellular function; to explore the role of epigenetic modifications and chromatin remodeling in nuclear architecture; to uncover mechanisms governing lineage specific 3D nuclear conformations and their perturbation in disease states; and to develop tools and databases to enable the study of the 3D nucleome.
- Bioelectronic Medicines: To establish precise and effective methods to stimulate the peripheral, autonomic, and enteric nervous systems and thereby control the function of physiologic systems and treat multiple diseases and conditions. This potential program, if implemented, will be DARPA-like in nature, representing a high risk, goal-driven endeavor to develop proof of concept for an entirely new class of neural control devices that have the potential to precisely treat a wide variety of diseases and conditions.
- Citizen Science: To assess the infrastructural and computational needs associated with direct engagement with the public in data collection, donation, and analysis; investigate

the ethical, legal, and social implications of biomedical research using citizen science methods.

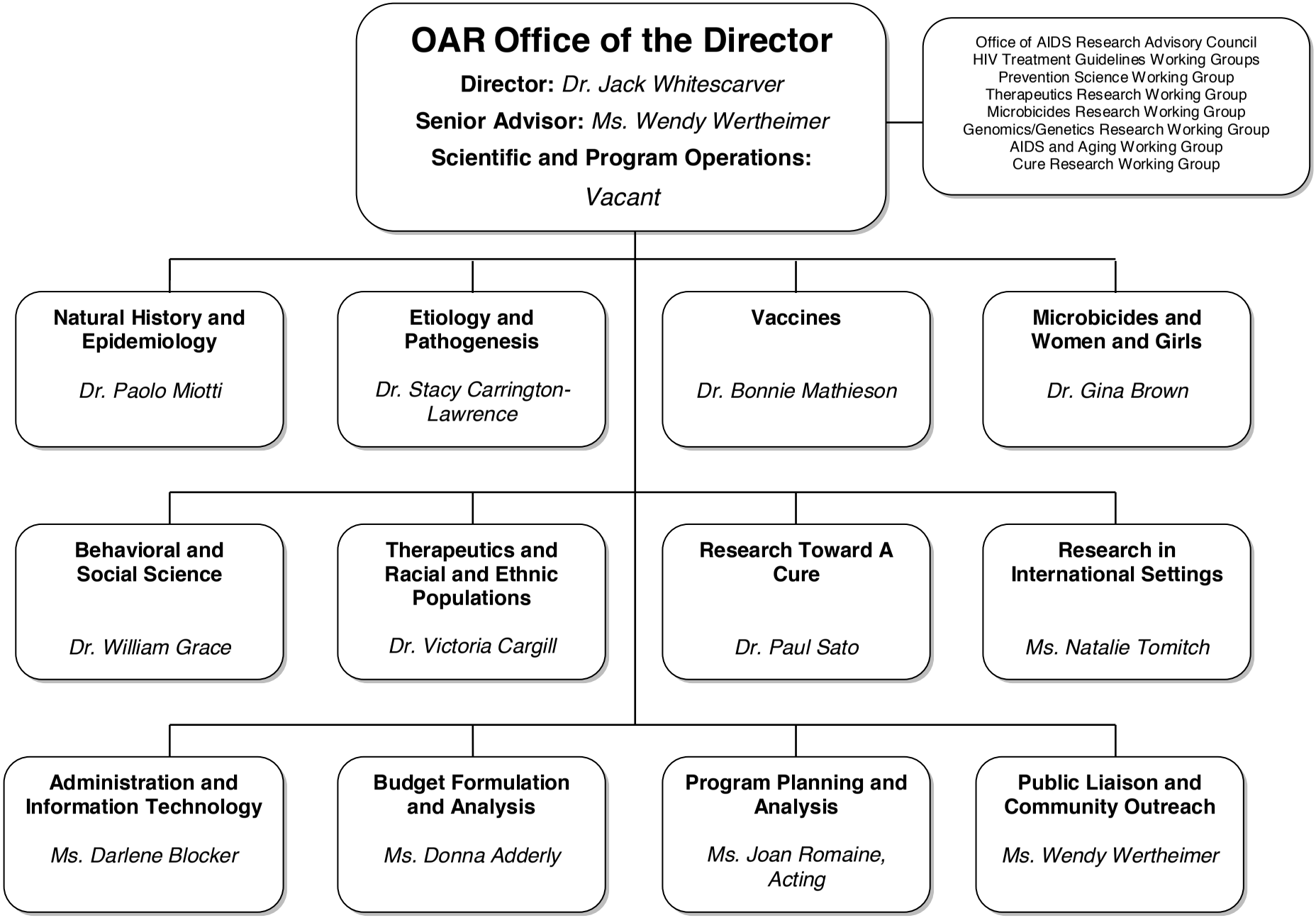
- Glycomics: To facilitate the functional analysis of sugar compounds which are attached to most proteins. Currently, such analyses require highly specialized expertise. This program, if implemented, would develop tools and methods that would extend the analysis to a wider group of scientists. .
- Mechanisms Underlying Benefits from Physical Activity: To explore the molecular and cellular mechanisms that underlie benefits of physical activity; to identify functions of genetic networks activated by physical activity; to determine common physiologic and biochemical mechanisms by which physical activity improves health and well-being, and the thresholds needed for benefits to occur; and to develop standardized protocols, tools, measures, etc. to allow for generalizability and meta-analyses.

Additionally, several Common Fund programs will be reaching the end of their first phase of support in FY 2014, and ongoing planning activities are assessing whether a second phase of funding is needed to reap maximum benefit from the program. The programs that may receive a second phase of funding beginning in FY 2015 are the Gulf Long-term Follow-up of Workers Study, Medical Education Partnership Initiative (within the Global Health program), and Science of Behavior Change.

Budget Policy:
In the FY 2015 President's Budget estimate, the Common Fund has $106.994 million available for new initiatives. Potential new initiatives will be selected through strategic planning activities designed to identify and understand ongoing work in each scientific area and to determine what opportunities exist for the Common Fund to have a significant impact.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Trans-NIH AIDS Research Budget


OAR Office of the Director
Director: Dr. Jack Whitescarver
Senior Advisor: Ms. Wendy Wertheimer
Scientific and Program Operations:
Vacant
Office of AIDS Research Advisory Council
HIV Treatment Guidelines Working Groups
Prevention Science Working Group
Therapeutics Research Working Group
Microbicides Research Working Group
Genomics/Genetics Research Working Group
AIDS and Aging Working Group
Cure Research Working Group
Natural History and Epidemiology
Dr. Paolo Miotti
Etiology and Pathogenesis
Dr. Stacy Carrington-Lawrence
Vaccines
Dr. Bonnie Mathieson
Microbicides and Women and Girls
Dr. Gina Brown
Behavioral and Social Science
Dr. William Grace
Therapeutics and Racial and Ethnic Populations
Dr. Victoria Cargill
Research Toward A Cure
Dr. Paul Sato
Research in International Settings
Ms. Natalie Tomitch
Administration and Information Technology
Ms. Darlene Blocker
Budget Formulation and Analysis
Ms. Donna Adderly
Program Planning and Analysis
Ms. Joan Romaine, Acting
Public Liaison and Community Outreach
Ms. Wendy Wertheimer

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Institute and Center
(Dollars in Thousands)

Institute / Center	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
NCI	$261,550	$269,923	$272,212	$2,289
NHLBI	64,046	64,218	64,559	341
NIDCR	18,896	18,465	17,873	-592
NIDDK	29,153	30,031	30,354	323
NINDS	44,136	45,465	44,223	-1,242
NIAID	1,481,620	1,567,913	1,590,026	22,113
NIGMS	61,415	64,263	64,956	693
NICHD	136,507	140,616	142,055	1,439
NEI	2,748	1,747	1,360	-387
NIEHS	5,028	5,179	5,151	-28
NIA	5,305	5,465	5,468	3
NIAMS	4,639	4,779	4,753	-26
NIDCD	1,768	1,821	1,811	-10
NIMH	179,449	157,493	157,005	-488
NIDA	300,749	301,532	300,714	-818
NIAAA	26,732	27,537	27,413	-124
NINR	11,908	12,266	12,202	-64
NHGRI	6,716	6,918	6,380	-538
NIBIB	3,484	1,229	713	-516
NIMHD	19,259	19,839	19,607	-232
NCCAM	1,516	1,562	1,415	-147
NCATS	64,360	66,297	64,287	-2,010
FIC	22,833	23,520	23,463	-57
NLM	7,220	7,937	7,897	-40
OD				
OAR	60,718	61,923	61,923	--
ORIP	76,110	77,153	77,153	--
Subtotal, OD	136,828	139,076	139,076	--
TOTAL, NIH	**$2,897,865**	**$2,985,091**	**$3,004,973**	**$19,882**

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS

(Dollars in Thousands)

MECHANISM	FY 2013 Actual		FY 2014 Enacted [2]		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,690	$1,096,653	1,528	$962,093	1,529	$1,193,973	1	$231,880
Administrative Supplements	*(99)*	100,494	*(47)*	16,610	*(43)*	16,010	*(-4)*	-600
Competing	571	256,261	712	609,380	741	402,205	29	-207,175
Subtotal, RPGs	2,261	$1,453,408	2,240	$1,588,083	2,270	$1,612,188	30	$24,105
SBIR/STTR	68	34,484	62	32,945	61	33,770	-1	825
Research Project Grants	2,329	$1,487,892	2,302	$1,621,028	2,331	$1,645,958	29	$24,930
Research Centers:								
Specialized/Comprehensive	62	$130,504	59	$127,380	59	$123,493	--	-$3,887
Clinical Research	2	55,673	2	57,209	2	55,617	--	-1,592
Biotechnology	0	759	0	778	0	720	--	-58
Comparative Medicine	16	56,560	16	56,703	16	56,341	--	-362
Research Centers in Minority Institutions	14	13,064	14	13,077	14	13,077	--	--
Research Centers	94	$256,560	91	$255,147	91	$249,248	--	-$5,899
Other Research:								
Research Careers	237	$42,034	235	$42,326	229	$42,068	-6	-$258
Cancer Education	0	0	0	0	0	0	--	--
Cooperative Clinical Research	8	17,550	8	17,550	8	17,550	--	--
Biomedical Research Support	1	2,672	1	2,672	1	2,672	--	--
Minority Biomedical Research Support	1	348	1	359	1	359	--	--
Other	152	61,981	155	60,147	152	59,440	-3	-707
Other Research	399	$124,585	400	$123,054	391	$122,089	-9	-$965
Total Research Grants	2,822	$1,869,037	2,793	$1,999,229	2,813	$2,017,295	20	$18,066
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	95	$3,993	93	$4,090	91	$3,993	-2	-$97
Institutional Awards	642	33,190	644	33,690	644	33,710	--	20
Total Research Training	737	$37,183	737	$37,780	735	$37,703	-2	-$77
Research & Develop. Contracts	107	$488,608	102	$434,001	102	$433,876	--	-$125
(SBIR/STTR) (non-add) [1]	*(3)*	*(688)*	*(6)*	*(1,659)*	*(7)*	*(4,047)*	*(1)*	*(2,388)*
Intramural Research		$325,775		$332,196		$333,463		$1,267
Res. Management and Support		116,544		119,962		120,713		751
Res. Management & Support (SBIR Admin) (non-add)								
Office of the Director - Appropriation [1]		*(136,828)*		*(139,076)*		*(139,076)*		--
Office of the Director - Other		60,718		61,923		61,923		--
ORIP (non-add) [1,3]		*(76,110)*		*(77,153)*		*(77,153)*		--
Total, NIH Discretionary B.A.		**$2,897,865**		**$2,985,091**		**$3,004,973**		**$19,882**

[1] All items in italics and brackets are non-add.

[2] The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

[3] Number of grants and dollar amounts for the ORIP component of the OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriation also is noted as a non-add since these funds are accounted for under OD-Other.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Activity
(Dollars in Thousands)

Area of Emphasis	FY 2011 Actual	FY 2012 Actual	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
HIV Microbicides	$120,982	$129,919	$111,240	$113,118	$112,647	-$471
Vaccines	548,834	556,613	518,170	530,866	535,187	4,321
Behavioral and Social Science	412,163	420,084	397,377	413,295	418,503	5,208
Etiology and Pathogenesis	730,978	668,244	625,027	664,954	693,985	29,031
Therapeutics						
Therapeutics as Prevention	*65,064*	*56,561*	*69,375*	*64,618*	*66,391*	*1,773*
Drug Discovery, Development, and Treatment	*615,475*	*650,059*	*632,123*	*663,839*	*652,157*	*-11,682*
Total, Therapeutics	680,539	706,620	701,498	728,457	718,548	-9,909
Natural History and Epidemiology	278,998	257,973	243,454	225,528	219,490	-6,038
Training, Infrastructure, and Capacity Building	232,624	280,775	261,921	269,912	267,139	-2,773
Information Dissemination	54,159	54,567	39,178	38,961	39,474	513
Total	**$3,059,277**	**$3,074,795**	**$2,897,865**	**$2,985,091**	**$3,004,973**	**$19,882**

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Justification of Budget Request

Office of AIDS Research
Trans-NIH AIDS Research Budget Justification
(see also: OAR section in Office of the Director/DPCPSI)

Budget Authority (BA):

FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015+/- FY 2014
$2,897,865,297	$2,985,091,000	$3,004,973,000	$19,882,000

DIRECTOR'S OVERVIEW

Groundbreaking Accomplishments: In the three decades since AIDS was first reported, the NIH has been the global leader in research to understand, prevent, diagnose, and treat HIV and its many related conditions. Recent scientific advances resulting from NIH-funded research represent a critical moment for AIDS research. New avenues for discovery have been identified, providing possibilities for the development of new strategies to prevent, treat, and potentially cure HIV. Recent accomplishments include:

- Development of new treatments for many HIV-associated co-infections, co-morbidities, malignancies, and clinical manifestations;
- Development of new strategies for the prevention of mother-to-child transmission (MTCT), which have resulted in dramatic decreases in perinatal HIV in the U.S., where now fewer than 100 babies a year are born with HIV infection;
- Demonstration of the first proof of concept that a vaccine can prevent HIV infection and identification of potential immune markers for protection;
- Discovery of more than 20 potent human antibodies that can stop up to 95 percent of known global HIV strains from infecting human cells in the laboratory;
- Demonstration that the use of antiretroviral therapy by infected individuals can dramatically reduce HIV transmission to an uninfected partner;
- Demonstration of the effectiveness of pre-exposure prophylaxis (PrEP), the use of antiretroviral treatment regimens by uninfected individuals to reduce their risk of HIV acquisition;
- Discovery that genetic variants may play a role in enabling some individuals, known as "elite controllers," to control HIV infection without therapy;
- Critical basic science discoveries that continue to provide the foundation for novel research;
- Advances in basic and treatment research aimed at eliminating viral reservoirs in the body that for the first time are leading scientists to design and conduct research aimed at a cure for HIV/AIDS.

In just the past few months, NIH intramural and extramural researchers have produced two new exciting advances. NIH researchers published the results of studies utilizing potent human

neutralizing antibodies that successfully suppressed a form of HIV in primates. This important research could potentially result in a new form of treatment for HIV that could be used as an adjunct to antiretroviral therapy and could lead to opportunities for novel research to treat and potentially cure HIV. NIH-sponsored researchers also have made tremendous strides in producing and analyzing proteins that may provide an important new pathway in AIDS vaccine design.

NIH is leading global research efforts to capitalize on all of these advances, move science forward, and begin to turn the tide against this pandemic. Despite this progress, the HIV/AIDS pandemic will remain the most serious global public health crisis of our time until better, more effective, and affordable prevention and treatment regimens—and eventually a cure—are developed and available around the world.

Mission: The NIH AIDS research program that produced these critical accomplishments is coordinated and managed by the Office of AIDS Research (OAR), which functions as an "institute without walls" with responsibility for AIDS-related research supported by every NIH Institute and Center (IC). OAR coordinates the scientific, budgetary, and policy elements of the trans-NIH research program on AIDS and its wide spectrum of associated malignancies, co-infections, and clinical complications. Through its unique trans-NIH planning, budget, and evaluation processes, OAR identifies the highest priority areas of scientific opportunity, enhances collaboration, and minimizes duplication to invest precious research dollars effectively. The OAR has shifted resources across ICs and areas of science as needed to address these priorities and the changing clinical profile of the pandemic.

Challenges and Opportunities for FY 2015: The key scientific priorities for NIH AIDS research address the goals of the President's National HIV/AIDS Strategy as well as the President's Executive Order about the HIV Care Continuum. The priorities are also aligned with the NIH Director's themes as outlined below. OAR will target funding on:

- **Today's Basic Science for Tomorrow's Breakthroughs**: A key priority is basic research on HIV that will underpin further development of critically needed *vaccines, microbicides, and other prevention strategies*. Another important area will focus on research related to the potential for a *cure or lifelong remission* of HIV infection, including studies on viral persistence, latency, reactivation, and eradication.

- **Precision Medicine:** NIH will continue to invest in research to *develop better, less toxic, longer acting, and sustained anti-HIV treatments* and to investigate how genetic determinants, sex, gender, race, age, nutritional status, treatment during pregnancy, and other factors interact to affect treatment success or failure. Research on behavioral issues, such as the role of stigma and adherence to treatment or prevention strategies, also is important, particularly to address the HIV Care Continuum. Another key priority in this area is research on *co-morbidities and disease progression*, including treatment and prevention of HIV-related co-infections, malignancies, and neurological, cardiovascular, and metabolic complications.

- **Nurturing Talent and Innovation:** NIH will utilize resources to train the next generation of AIDS researchers around the world to foster collaboration and innovation in AIDS research, with a particular emphasis on *research toward a cure.*

Overall Budget Policy:

To address these critical AIDS research priorities, the FY 2015 President's Budget estimate for the trans-NIH AIDS research program is $3,004.973 million, an increase of $19.882 million or 0.7 percent above the FY 2014 Enacted level. This amount includes the total trans-NIH support for intramural and extramural research for basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the wide spectrum of AIDS-associated malignancies, opportunistic infections, co-infections, and clinical complications; as well as research management support; research centers; and training and infrastructure. This request reflects the shifting of funds across ICs to address new and exciting scientific opportunities in AIDS research. These shifts reflect the scientific priorities identified through the unique annual trans-NIH strategic planning portfolio analysis, and budget processes and address the evolving clinical profile of the epidemic, changing demographics, and most recent scientific advances. In this budget request, OAR has provided increased funding to support: high priority basic research (etiology and pathogenesis) that provides the underlying foundation for all HIV research, including prevention and treatment of HIV and research to better understand disease progression and HIV-related co-morbidities. This fundamental research also includes the first year of a three-year commitment to increase NIH research toward a cure. Another major priority is prevention research, particularly new opportunities in the development of vaccines. An increase is provided for behavioral and social sciences research, particularly research to better understand issues of adherence to both prevention and treatment strategies. In order to provide those increases to support the highest priorities and new scientific opportunities, OAR has had to reduce and redirect funds from other scientific areas within AIDS research.

PROGRAM DESCRIPTIONS AND ACCOMPLISHMENTS

Trans-NIH Strategic Plan and Budget: This budget request is informed by the FY 2015 Trans-NIH Plan for HIV-Related Research (Strategic Plan). The OAR trans-NIH planning process involves government and non-government experts and representatives from community constituency groups. This process results in the identification of overarching AIDS-research priorities and specific research objectives and strategies. The OAR Advisory Council has also reaffirmed the key scientific priorities. OAR is mandated to develop the annual trans-NIH AIDS research budget in partnership with the ICs and explicitly tied to the objectives of the Strategic Plan. OAR's AIDS research allocation to each IC is not based on a formula, but on the scientific priorities and objectives of the annual Strategic Plan, taking into account the current scientific opportunities and priorities, the evolving clinical profile of the epidemic, and the IC's capacity to absorb and expend resources for the most meritorious science. This process reduces redundancy, promotes harmonization, and assures cross-Institute collaboration to conduct and support research in domestic and international settings. Specific programmatic areas include:

HIV MICROBICIDES

A safe and effective microbicide will be an important asset to the HIV prevention tool kit. Microbicides are products, including antiretroviral drugs and other agents, which could be applied topically or injected to prevent acquisition of HIV and other sexually transmitted infections. Microbicides could be used alone or in combination with other strategies. NIH supports a comprehensive and innovative microbicide research program that includes the screening, discovery, development, preclinical testing, and clinical evaluation of microbicide candidates. NIH supports basic science research aimed at understanding how HIV crosses mucosal membranes and infects cells. In addition, NIH supports behavioral and social science research on adherence to, and the acceptability and use of microbicides among different populations. These projects include the safety of microbicide use during pregnancy and menopause; studies in adolescents and in men who have sex with men; and implementation research to better understand how to integrate a potential product into community prevention practices. Basic science and clinical studies have shown promise for the use of antiretroviral (ARV)-based microbicides as HIV prevention strategies. Follow-up studies are underway or being developed to test different ARV- and non-ARV-based products, microbicides combined with a contraceptive for multipurpose prevention, and microbicides combined with antimicrobial agents to prevent HIV and other sexually transmitted infections (STIs). Microbicide formulations and new technologies that enhance adherence, such as injectable products, nanofibers, films, suppositories, and intravaginal rings also are being developed and studied.

Budget Policy:

The FY 2015 President's Budget request for Microbicides research is $112.647 million, a decrease of $0.471 million or 0.4 percent below the FY 2014 Enacted level for this area of prevention research. In FY 2015, NIH will continue to support the discovery, design, development, formulation, and evaluation of microbicide candidates. Key ongoing activities include support for the NIH-funded Microbicide Trials Network (MTN) and the necessary infrastructure to conduct basic research and microbicide clinical trials. Research activities will utilize this infrastructure to build on recent scientific advances and develop innovative, novel, and high risk-high reward approaches for the discovery, development, formulation, and testing of microbicide candidates and delivery systems. Research activities also will focus on the development and testing of multi-purpose prevention technologies (MPTs) that prevent HIV and other STIs or HIV and pregnancy; and on the continued study of animal and tissue models designed to enhance understanding of the mechanisms of HIV infection and assist safety and efficacy evaluations of candidate microbicide products. NIH will support research needed for the development of criteria for the selection of candidate microbicides to be advanced through the different phases of preclinical and clinical studies including clinical safety and effectiveness studies and research on ethics, adherence, and other behavioral and social science issues that can impact clinical trials and microbicide use. Through a number of trans-governmental working groups and non-governmental expert consultations, OAR will continue to foster coordination and

collaboration in innovative microbicide research leading to the development and testing of novel potential candidates that can prevent HIV transmission and acquisition.

VACCINES

The best long-term hope for controlling the AIDS pandemic is the development of safe, effective, and affordable AIDS vaccines that may be used in combination with other prevention strategies. NIH supports a broad AIDS vaccine research portfolio encompassing basic, preclinical, and clinical research, including studies to identify and better understand potentially protective immune responses in HIV-infected individuals and studies of improved animal models for the preclinical evaluation of vaccine candidates. Information gained from these studies is being used to inform the design and development of novel vaccine strategies. Since the modest success of the RV144 trial in Thailand using a pox virus vector and HIV envelope protein boosts, NIH has supported unprecedented international collaborative investigations to identify how specific immune responses may protect against HIV acquisition. Samples from the HVTN 505 trial in the U.S. with DNA and adenovirus vectors are being subjected to similar analyses to understand why that vaccine strategy failed to protect against HIV acquisition. To build on the knowledge gained from these studies, clinical trials in other populations and in other parts of the world with new and potentially improved products and alternative vectors have been designed and are currently underway. Recent data from several phase I and II vaccine clinical studies present new scientific opportunities for the development of improved HIV vaccine candidates.

Budget Policy:

The FY 2015 President's Budget request for Vaccine research is $535.187 million, an increase of $4.321 million or 0.8 percent above the FY 2014 Enacted level. Innovative basic HIV vaccine research studies will be supported to inform the development of new vaccine concepts that might prevent HIV infection more efficiently than vaccines already tested. In FY 2015, NIH will fund additional development of improved animal models including new models for vaccine challenge studies in non-human primates to test vaccine concepts and to aid informed testing of HIV vaccine candidates in clinical trials. NIH will provide support for new initiatives to integrate systems biology with HIV vaccine discovery; and will fund additional research to develop new tests to measure immune responses to the HIV vaccine candidate that will more closely predict outcomes of parallel preclinical animal and human clinical studies. Resources will be directed toward the development and testing of improved vaccine candidates in additional clinical studies, both in the U.S. and abroad, building on the early protection observed in the previous Phase III vaccine trial in Thailand and a deeper understanding of the failure of the recent HVTN 505 trial to demonstrate protection in clinical trial participants in the U.S. To ensure that these new opportunities can be pursued, a realignment of resources will be needed. This budget request reflects OAR's redirection of funds from other scientific areas to support critical vaccine research opportunities.

BEHAVIORAL AND SOCIAL SCIENCE

As studies continue to define a role for the use of antiretroviral medications for HIV prevention, NIH is supporting research to understand how these drugs can best be used for prevention in specific populations and social contexts. NIH will continue to study ways to change those behaviors and social contexts and to facilitate engagement and retention in HIV testing, prevention, and treatment services. NIH is supporting research to address factors associated with the HIV Care Continuum, and specifically on HIV care outcomes. Investigations are not only focused on individual-level variables, but on social and structural issues, such as the role of stigma, housing, employment, health care access, and interpersonal networks. Studies have suggested that modifying these variables can promote early access to medical care, reduce costs, extend life expectancy, and improve quality of life. NIH will continue to develop new research methods that can be applied to behavioral and social science studies, as well as the integration of biomedical and behavioral strategies in clinical investigations. These include approaches to increase recruitment into clinical trials; enhance statistical analyses of behaviors, such as alcohol use, that can affect medication studies; and identify behavioral issues relevant to genetic or genomic studies.

Budget Policy:

The FY 2015 President's Budget request for Behavioral and Social Science is $418.503 million, an increase of $5.208 million or 1.3 percent above the FY 2014 Enacted level. NIH will shift its investments within the area of behavioral and social sciences to keep pace with the increasing integration of biomedical and behavioral perspectives, the success of antiretroviral medications in both prevention and treatment, and the key role of adherence to this success. To achieve a more integrated portfolio, attention will be given to improving the implementation of therapies in specific populations and social contexts. Social variables, such as stigma, and structural variables to improve access to prevention and treatment resources will also be addressed, and a strong emphasis on basic science to understand risk behaviors from both a social and biomedical (e.g., neurophysiologic and genomic) perspective. NIH will support initiatives to better understand the multiple factors related to adherence, utilizing novel ways to ensure that patients take their medications and use prevention strategies appropriately.

ETIOLOGY AND PATHOGENESIS

NIH supports a comprehensive portfolio of research focused on the transmission, acquisition, establishment, and maintenance of HIV infection and the causes of its associated profound immune deficiency and severe clinical complications. Research on basic HIV biology and AIDS pathogenesis has revolutionized the design of drugs, methodologies for diagnosis of HIV infection, and tools for monitoring disease progression and the safety and effectiveness of antiviral therapies. Ground-breaking strides have been made towards understanding the fundamental steps in the life-cycle of HIV, the host-virus interactions, and the clinical manifestations associated with HIV infection and AIDS. Additional research is needed to further the understanding of the virus and how it causes disease, including studies to delineate how sex, gender, age, ethnicity, race, pregnancy, nutritional status, and other factors interact to influence vulnerability to infection and disease progression; determine the role of immune dysfunction and chronic inflammation in HIV pathogenesis; and further the understanding of the development of HIV-associated co-morbidities, such as cardiovascular, neurological, and other clinical complications, malignancies, and co-infections (including tuberculosis [TB] and hepatitis C). Research examining the genetic determinants associated with HIV susceptibility, disease progression, and treatment response is also needed. These studies may lead to the development of customized therapeutic and preventive regimens formulated for an individual patient based on his or her genetic sequence. NIH also prioritizes research examining the mechanisms by which HIV establishes and reactivates latent reservoirs of infection and studies that further the understanding of factors that are associated with the ability of the host to restrict HIV infection and/or mitigate HIV disease progression. A better understanding of these processes could help identify key targets for the development of new therapeutic and vaccine strategies to prevent or control HIV infection and possibly lead to a cure for HIV disease.

Budget Policy:

The FY 2015 President's Budget request for the basic research area of Etiology and Pathogenesis is $693.985 million, an increase of $29.031 million or 4.4 percent above the FY 2014 Enacted level. Studies related to the development of microbicides and vaccines, as well as research toward a cure have revealed gaps in knowledge and understanding of HIV etiology and pathogenesis, particularly with regard to host immune responses, how HIV interacts with and crosses host target surfaces, and the establishment and maintenance of latent viral reservoirs in the body (HIV persistence). NIH will provide increased resources for research on the biology of HIV transmission and pathogenesis studies including research on HIV-associated immune system dysfunction and chronic inflammation. NIH will support studies of clinical complications, such as HIV-associated co-infections, malignancies, premature aging, cardiovascular disease, neurological and metabolic disorders. Funds will be provided for research to better understand the differences in HIV transmission, treatment, and progression in women compared to men as well as the unique clinical manifestations of HIV disease in women. An important area will focus on research related to the potential for a cure or lifelong remission of HIV infection, including studies on viral persistence, latency, and reactivation. On World

AIDS Day 2013, the President announced that NIH will redirect $100 million over the next three fiscal years (FY 2015-2017) to research towards a cure. OAR will launch that new initiative with an investment of $15 million in cure research in FY 2015. OAR jump-started the initiative with an investment of an additional $10 million in FY 2014.

Program Portrait: Research Toward a Cure: Eradication of Viral Reservoirs

FY 2014 Level: $ 88.5 million
FY 2015 Level: $104.9 million
Change: $+16.4 million

Research related to the potential for a cure or lifelong remission of HIV infection is a key NIH research priority, which currently involves research across a number of areas. NIH plans to increase this area of research over the next three fiscal years focused on:

- **Pathogenesis studies:** Basic research on viral reservoirs, viral latency, and viral persistence, including studies on genetic factors associated with reactivation of the virus, and other barriers to HIV eradication.
- **Animal models:** Identification and testing of various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.
- **Drug development and preclinical testing:** Programs to develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system and brain.
- **Clinical trials:** Studies to evaluate lead compounds, drug regimens, and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.
- **Therapeutic vaccines:** Design and testing of vaccines that would be capable of suppressing viral replication and preventing disease progression.
- **Adherence/compliance:** Development and testing of strategies to maintain adherence/compliance to treatment, in order to improve treatment outcomes and reduce the risk of developing HIV drug resistance.

THERAPEUTICS

Drug Discovery, Development and Treatment: Antiretroviral treatment (ART) has resulted in improved immune function in patients who are able to adhere to the treatment regimens and tolerate the toxicities and side effects associated with antiretroviral drugs. ART also has delayed the progression of HIV disease to the development of AIDS. Unfortunately, the treatment is beginning to fail in an increasing number of patients who have been on antiretroviral therapy. These patients are experiencing serious drug toxicities and

Improved Therapies for Long-Term Survival

NIH researchers are working to:

- Develop innovative therapies and novel cell-, gene-, and immune-based approaches to control and eradicate HIV infection;
- Develop new formulations, including long-acting therapies;
- Identify new drug targets based on the structure of HIV/host complexes;
- Delineate the interaction of aging and AIDS, including neurological, cardiovascular, and metabolic complications, as well as issues of frailty;
- Discover and develop improved therapies for AIDS-defining and non-AIDS-defining malignancies; and
- Discover the next generation of drugs that may be used in potential “therapeutics as prevention” strategies.

developing drug resistance. Recent epidemiologic studies have shown that the incidence of co-infections, co-morbidities, AIDS-defining and non-AIDS defining malignancies, and complications associated with long-term HIV disease and ART are increasing. These include tuberculosis, Hepatitis C, metabolic disorders, cardiovascular disease, conditions associated with aging, and neurologic and neurocognitive disorders. NIH supports a comprehensive therapeutics research program to design, develop, and test drugs and drug regimens. Under development are new combinations of drugs and sustained release formulations and delivery systems to maintain undetectable viral load, to overcome drug resistance and treatment failure, and to prevent and treat HIV-associated co-infections, co-morbidities, and other complications. The program supports cure research with a focus on developing drugs and cell- and gene-based strategies that can target and eradicate persistent viral reservoirs in various cells, tissues, and organ systems, including the central nervous system and brain. This program also is supporting pre-clinical trials of innovative strategies to eliminate viral reservoirs including testing therapeutic anti-HIV monoclonal antibodies with and without antiretroviral drugs.

Therapeutics as Prevention: A critical new area of prevention research is the study of treatment strategies as a method to prevent new HIV infections. This approach builds on NIH-sponsored landmark clinical trials that demonstrated that treatment of HIV-infected pregnant women could significantly reduce transmission of HIV from mother to child. Recent groundbreaking studies have demonstrated the successful use of antiretrovirals to prevent transmission of HIV in specific populations. Clinical results from a large NIH-sponsored international clinical trial (HIV Prevention Trials Network [HPTN] 052) showed that early initiation of antiretroviral treatment of HIV-infected heterosexual individuals resulted in a 96 percent reduction in sexual transmission of HIV to their uninfected partner. Another major NIH-sponsored clinical trial, the Chemoprophylaxis for HIV Prevention in Men study, also known as iPrEx, demonstrated that daily use of an antiretroviral drug by some high-risk uninfected men could reduce their risk of acquiring HIV. The findings from this study showed proof of concept and the effectiveness of a novel HIV prevention strategy known as Pre-Exposure Prophylaxis (PrEP). Recent studies have shown PrEP to be effective in preventing HIV acquisition among two at-risk populations: women in heterosexual discordant couples and injection drug users. NIH supports ongoing basic, translational, clinical, and implementation research to develop combinations of antiretroviral drugs and compounds that can be used in sustained release formulations that can be used in potential new PrEP strategies; test PrEP in high risk uninfected populations, including adolescents; evaluate post-exposure prophylaxis, the use of ART to prevent infection after HIV exposure, including in a healthcare setting; develop improved regimens to prevent mother-to-child transmission; and evaluate a potential innovative prevention strategy known as “test and treat” to determine the impact of increased testing with immediate referral to treatment at the community level.

Budget Policy:

The FY 2015 President’s Budget request for Therapeutics research is $718.548 million, a decrease of $9.909 million or 1.4 percent below the FY 2014 Enacted level. The overall funding for therapeutics research will be reduced to allow for increased funding for other areas. A portion of the funds from expiring grants and contracts for therapeutics research will be reallocated to studies on treatment and prevention of HIV-associated co-infections and co-morbidities and to support crucial basic research on targeting and eradicating HIV reservoirs.

Resources within the area of Therapeutics also will be directed to support: recompetition of the AIDS Malignancy Consortium and Pediatric HIV/AIDS Cohort Study; development of new combinations of anti-HIV drugs and sustained release formulations and delivery systems to maintain viral suppression; several initiatives to develop and test new therapeutic monoclonal antibodies with and without antiviral drugs; expansion of programs targeting innovative approaches to develop and evaluate novel cell-, gene-, and immune-based approaches to control and eradicate HIV infection that may lead to a cure; identifying new drug targets based on the structure of HIV/host complexes; delineating the interaction of aging and neuro-AIDS; developing new strategies to test and treat patients with HIV-related co-infections, including Hepatitis C virus and tuberculosis; and conducting clinical studies on cardiovascular complications of HIV disease and ART. Increased funding will be provided for the area of *Therapeutics as Prevention*, including discovery and testing the next generation of sustained release formulations of antiretroviral drugs that may be used in potential new strategies for PrEP; treatment of HIV-infected individuals to prevent transmission; post-exposure prevention; and new antiretroviral drug regimens to prevent mother-to-child transmission, including transmission through breastfeeding.

NATURAL HISTORY AND EPIDEMIOLOGY

Natural history and epidemiologic research on HIV/AIDS is critical to the monitoring of epidemic trends, evaluation of prevention modalities, characterization of the clinical manifestations of HIV disease, and measurement of the effects of treatment regimens at the population level. Novel methodologies in the area of biostatistics, mathematical modeling, and laboratory technology have provided the basis for new epidemiological approaches in addressing HIV/AIDS. Multi-site epidemiologic studies in the U.S. are identifying new HIV-related co-morbidities and helping to differentiate effects related to antiretroviral treatment from those related to HIV disease. As the AIDS epidemic continues to evolve, there is a crucial need for epidemiologic studies in domestic and international settings. NIH supports a comprehensive research portfolio in both settings to study the epidemiologic characteristics of populations in which HIV is transmitted and the changing spectrum of HIV-related disease (including the occurrence of co-infections, malignancies, metabolic, cardiovascular, neurological, skeletal, and other complications). These studies have delineated the significant health disparities that are critical factors in the epidemic (e.g., racial and ethnic disparities in the U.S.; between industrialized and resource-constrained nations; between men and women; and health disparities based on sexual identity). Ongoing observational studies are adding focus on at-risk individuals from the rural South in the U.S. as well as individuals over the age of 50. Research on HIV-related health disparities and their impact on treatment access and effectiveness, as well as HIV prevention, will continue to be an NIH AIDS research priority.

Budget Policy:

The FY 2015 President's Budget request for Natural History and Epidemiology is $219.490 million, a decrease of $6.038 million or 2.7 percent below the FY 2014 Enacted level. The funding reduction in this area will allow OAR to shift these funds to key priorities within prevention research and research toward a cure. However, NIH will continue to use existing

networks and research cohorts to support high-priority epidemiology studies of populations most at risk, including men who have sex with men (MSM), especially MSM of color; women; adolescents; and individuals over fifty years of age who are aging with HIV. Population studies on the long-term effects of HIV disease and its treatment will be emphasized as well as studies of non-communicable disease co-morbidities that have become more commonly diagnosed in HIV-infected people under HIV treatment. Epidemiologic research also will include the development of novel trans-disciplinary methods to examine the prevention, testing, and treatment cascade by integration of data from electronic medical records, observational studies, clinical trials and simulation, mathematical modeling, and molecular epidemiology. Resources will be provided for studies of HIV implementation science, including those that advance new methodologies and studies that maximize program effectiveness by addressing organizational and system-level barriers to the scale-up of prevention and treatment interventions. Studies also will be supported that formally evaluate the economic impact and cost-effectiveness of diverse interventions strategies in different regions and circumstances.

TRAINING, INFRASTRUCTURE, AND CAPACITY BUILDING

NIH supports the training of domestic and international biomedical and behavioral HIV researchers. NIH also provides infrastructure and capacity building support as integral aspects of its commitment to carrying out scientifically and ethically sound and highly productive HIV-related research. The expansion of NIH-funded HIV research globally has necessitated the development of research training and infrastructure and capacity building efforts in many resource-limited settings throughout the world. NIH-funded programs have increased the number of training positions for HIV-related researchers, including domestic and international programs specifically designed to recruit individuals from populations underrepresented in research into research careers and to build research capacity at minority-serving institutions in the U.S. Equipment, shared instrumentation, and tissue and specimen repositories are examples of the research infrastructure and capacity building support that NIH provides to strengthen the conduct of AIDS-related research, both domestically and internationally.

Budget Policy:

The FY 2015 President's Budget estimate for Training, Infrastructure, and Capacity Building is $267.139 million, a decrease of $2.773 million or 1.0 percent below the FY 2014 Enacted level. NIH will continue to support training programs and infrastructure development for both U.S. and international researchers to build the critical capacity to conduct AIDS research in the United States and in developing countries. NIH will continue to build capacity for the development of animal models for AIDS research by continuing to support ongoing efforts to increase the supply of non-human primates and develop other animal models. NIH will support efforts to ensure an adequate number of trained intramural AIDS researchers through the AIDS Research Loan Repayment Program and the Intramural AIDS Research Fellowship program.

INFORMATION DISSEMINATION

NIH supports initiatives to enhance dissemination of research findings; develop and distribute state-of-the-art treatment and prevention guidelines; and enhance recruitment and retention of participants in clinical studies. Effective information dissemination approaches are an integral component of HIV prevention and treatment efforts. These efforts are crucial in light of the advent of new and complex antiretroviral treatment regimens, issues related to adherence to prescribed treatments, and the need to translate behavioral and social prevention approaches into practice. The changing pandemic and the increasing number of new infections in specific population groups in the U.S. underscore the need to disseminate HIV research findings and other related information to communities at risk, such as racial and ethnic populations, women, older individuals, and men who have sex with men. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to use new and emerging technologies to speed the translation of research results into practice and to shape future research directions.

Budget Policy:
The FY 2015 President's Budget estimate for Information Dissemination is $39.474 million, an increase of $0.513 million or 1.3 percent above the FY 2014 Enacted level. As the number and complexity of clinical studies increases, resources must be invested in clinical trials-related information dissemination to ensure recruitment of an adequate number of participants, particularly from populations at risk, including women and racial and ethnic populations in the United States. Funding also will be provided to ensure that clinical trial information and critical federal guidelines on the use of antiretroviral therapy, as well as guidelines for the management of HIV complications for adults and children, are updated regularly and disseminated widely to healthcare providers and patients through the AIDS*info* website (www.aidsinfo.nih.gov).

Global Impact of NIH AIDS Research: Research to address the global pandemic is essential. AIDS research represents the largest component of the total NIH global research investment. Since the early days of the epidemic, NIH has maintained a strong international AIDS research portfolio that has grown to include projects in approximately 100 countries around the world. NIH AIDS research studies are designed so that the results are relevant for both the host nation and the U.S. These research programs also enhance research infrastructure and training of in-country scientists and healthcare providers. New collaborations have been designed to improve both medical and nursing education as a mechanism to build a cadre of global health leaders. Most of these grants and contracts are awarded to U.S.-based investigators to conduct research in collaboration with in-country scientists; some are awarded directly to investigators in international scientific, academic, or medical institutions.

AIDS Research Conducted in International Settings
(Dollars in Millions)

FY 2013 Actual	FY 2014 Enacted	FY 2015 PB
$389.166	$ 375.826	$375.870

Benefits of AIDS Research to Other Areas: It is essential to point out that AIDS research also pays extensive dividends in many other areas of biomedical research, including in the prevention, diagnosis, and treatment of many other diseases. It deepens our understanding of immunology, virology, microbiology, molecular biology, and genetics. AIDS research is helping to unravel the mysteries surrounding so many other diseases because of the pace of discovery and the unique nature of HIV, i.e., the way the virus enters a cell, causes infection, affects every organ system, and unleashes a myriad of opportunistic infections, co-morbidities, cancers, and other complications. AIDS research continues to make discoveries that can be applied to other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia. AIDS treatment research has led to more effective drugs for multiple bacterial, mycobacterial, and fungal diseases and fostered significant improvements in drug design technologies. AIDS research has led to the development of new models to test treatments for other diseases in faster, more efficient, and more inclusive clinical trials. Drugs developed to prevent and treat AIDS-associated opportunistic infections also now benefit patients undergoing cancer chemotherapy and patients receiving anti-transplant rejection therapy. AIDS research also has advanced understanding of the relationship between viruses and cancer. New investments in AIDS research will continue to fuel biomedical advances and breakthroughs that will have profound benefits far beyond the AIDS pandemic.

Conclusion: Despite the groundbreaking scientific advances that have resulted from the NIH investment in AIDS research, many serious challenges lie ahead. There is little doubt that the AIDS pandemic will continue to impact virtually every nation in the world for decades to come. In light of this reality, the U.S. national commitment to AIDS research remains strong. The NIH will continue to build on this important moment in science and to support critical research to find new tools to turn the tide in the fight against this pandemic so that we can all once again live in a world without AIDS.

Department of Health and Human Services

National Institutes of Health

Drug Control Programs

FY 2015 Budget | Page No.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Resource Summary

	Budget Authority ($ in Millions)		
	FY 2013 Actual	**FY 2014 Enacted**	**FY 2015 President's Budget**
Drug Resources by Function			
Research and Development: Prevention	$390.255	$403.667	$406.222
Research and Development: Treatment	663.748	675.533	680.492
Total Drug Resources by Function	**$1,054.003**	**$1,079.200**	**$1,086.714**
Drug Resources by Decision Unit			
National Institute on Drug Abuse [1]	$992.225	$1,015.754	$1,023.268
National Institute on Alcohol Abuse and Alcoholism	61.778	63.446	63.446
Total Drug Resources by Decision Unit	**$1,054.003**	**$1,079.200**	**$1,086.714**

Drug Resources Personnel Summary			
Total FTEs (direct only)	394	394	394
Drug Resources as a Percent of Budget			
Total Agency Budget Authority (in Billions)	$29.001	$30.003	$30.203
Drug Resources Percentage	3.63%	3.60%	3.60%

[1] Comparable Budget Authority in FY 2013 and FY 2014

Program Summary

MISSION

National Institute on Drug Abuse (NIDA)

The societal impact of substance abuse (alcohol, tobacco, illicit and nonmedical use of prescription drugs) in this country is daunting, exceeding $600 billion a year in health care, crime-related, and productivity losses. Knowledge is the foundation of the transformative agenda needed to strike at the heart of this stubborn and costly challenge. To provide a comprehensive public health response, NIDA will continue to build on science advances from our investments in genetics, neuroscience, pharmacotherapy, and behavioral and health services research that have led to innovative strategies for preventing and treating substance abuse and addiction in this country and worldwide.

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Since its creation, NIAAA has led efforts to define alcohol issues as medical in nature and address them using evidence-based findings. The work supported by the Institute has transformed the understanding of alcohol abuse and dependence and their treatment. NIAAA provides leadership in the national effort to reduce alcohol-related problems, including underage drinking by: conducting and supporting research in a wide range of scientific areas including genetics, neuroscience, epidemiology, health risks and benefits of alcohol consumption, prevention, and treatment; coordinating and collaborating with other research institutes and Federal programs on alcohol-related issues; collaborating with international, national, state, and local institutions, organizations, agencies, and programs engaged in alcohol-related work; and translating and disseminating research findings to health care providers, researchers, policymakers, and the public.

Collaborative Research on Addiction at NIH (CRAN)

NIH established the Collaborative Research on Addiction at NIH (CRAN) in FY 2013 to facilitate collaborative research across Institutes on substance use, abuse, addiction, and their related health consequences. The National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), and the National Cancer Institute are the lead Institutes; participation by other NIH Institutes/Centers (ICs) is encouraged for relevant initiatives.

METHODOLOGY

NIDA's entire budget is drug-related and therefore scored as a part of the National Drug Control Budget.

The NIAAA prevention and treatment components of its underage drinking research are scored as a part of the National Drug Control Budget. Underage drinking research is defined as research that focuses on alcohol use, abuse and dependence in minors (children under the legal drinking age of 21). It includes all alcohol related research in minors, including behavioral research, screening and intervention studies and longitudinal studies. Beginning with the reporting of FY 2010 final budget authority, NIAAA's methodology for developing budget estimates for the *Budget and Performance Summary* uses the NIH research categorization and

disease coding (RCDC) fingerprint for underage drinking that allows for an automated categorization process based on electronic text mining to make this determination. Once all underage drinking projects and associated amounts are determined using this methodology, NIAAA conducts a manual review and identifies just those projects and amounts relating to prevention and treatment. This subset makes up the NIAAA drug control budget estimate.

BUDGET SUMMARY

The FY 2015 Request is $1,086.7 million for NIH's drug budget related activities, which is an increase of $7.5 million above the FY 2014 level. NIH-supported research has and will continue to provide the scientific basis for budget policy. For example, NIH continues to explore the many influences on drug addiction vulnerability, including genetics and epigenetics, which will allow the development of more targeted and effective prevention approaches. Research reveals that universal prevention programs not only reduce drug abuse, underage drinking, and other risky behaviors that can lead to HIV and other adverse outcomes, but can also promote other positive outcomes, such as strengthening young people's sense of community, or "connection" to school—key to reducing drug use, violence, and mental health problems.

Another top priority continues to be the development of medications to treat addiction, with NIH now poised to capitalize on a greater understanding of the neurobiology underlying addiction and of newly identified candidate systems and molecules as medication targets. NIH is also exploring ways in which health care reform, and the Affordable Care Act (ACA) specifically, can help bring people who have been marginalized, such as those with substance use problems, HIV, or both, into a network of care, and generate a major public health impact.

National Institute on Drug Abuse

The FY 2015 Request is $1,023.3 million for NIDA, which is an increase of $7.5 million above the FY 2014 level. NIDA's efforts consist of Epidemiology, Services and Prevention Research, Basic and Clinical Neuroscience Research, Pharmacotherapies and Medical Consequences, Clinical Trials Network, the Intramural Research Program (IRP), and Research Management and Support (RM&S). Each is discussed below.

Epidemiology, Services and Prevention Research (FY 2015 Request: $253.8 million)

This NIDA Division supports integrated approaches to understand and address the interactions between individuals and environments that contribute to drug abuse-related problems. It supports large surveys (e.g., the annual Monitoring the Future Survey, which tracks drug use and related attitudes among teens) and surveillance networks (e.g., the Community Epidemiology Work Group) to monitor drug-related issues and trends locally and nationally. Program efforts help identify substance abuse trends locally, nationally, and internationally; guide development of responsive interventions for a variety of populations; and encourage optimal service delivery in real-world settings. For example, factors associated with marijuana use have been undergoing dramatic changes. The potency, sources, availability, public perception, and legal status are significantly different than when marijuana use became a national issue more than 40 years ago. NIDA plans to support research to better understand the longer term outcomes resulting from these changes, such as trends in use, harm perception, clinical/social consequences, brain development, educational outcomes, and market/demographic variables, particularly for

adolescents and young adults. Such knowledge can be then used to inform policy, the public, and to improve prevention and treatment interventions.

Basic and Clinical Neuroscience Research (FY 2015 Request: $440.7 million)
The Basic and Clinical Neuroscience programs work together to expand understanding of the neurobiological, genetic/epigenetic, and behavioral factors that underlie drug abuse and addiction. Specifically, they examine which variables influence risk of drug abuse, addiction, and drug-related disorders; how addiction works in the brain, including the effects of drugs on the expression or silencing of genes; and how resultant changes affect brain function and consequent behaviors. Collectively, this research provides critical information to develop and test novel prevention and treatment interventions for drug abuse and addiction. For example, as mentioned above, a pressing research priority that has recently emerged due to the rapidly changing political and legal landscape surrounding marijuana, is the need to improve our understanding of the role of the endocannabinoid system in brain development, function and activity and the impact of marijuana use on these processes (particularly among young people). This Division also supports fundamental research to better understand brain function. For example, our knowledge of the various mechanisms the brain uses to fuel its operations (i.e., brain energetics) is surprisingly limited. Energy utilization patterns in the brain enable and shape all mental and behavioral activities, both normal and pathological. Brain energy utilization (and thus behavior) is profoundly affected by environmental conditions, such as diet, stress and exposure to drugs of abuse. NIDA is, therefore, soliciting grant applications to improve our basic understanding of the molecular mechanisms whereby chronic exposure to drugs of abuse impacts brain energetics. Successful projects are poised to identify new molecular targets that could be harnessed to design novel medications and/or behavioral treatments for addiction.

Pharmacotherapies and Medical Consequences (FY 2015 Request: $133.0 million)
This program area is responsible for medications development aimed at helping people recover from drug abuse and addiction and sustain abstinence. For example, this Division is encouraging the formation of strategic alliances to leverage NIDA resources between collaborating organizations (such as academic institutions, pharmaceutical and biotechnology companies) with the common goal of advancing medications through the development pipeline toward Food and Drug Administration (FDA) approval, in a timely manner. This Division also includes programs to address the medical consequences of drug abuse and addiction, including infectious diseases such as Hepatitis C virus (HCV) and HIV. Because of the high co-occurrence of substance abuse and infectious diseases, infectious disease specialists have a role to play in ensuring that their HIV+/HCV+ patients receive treatment for their substance-use disorders. NIDA plans to support research to address this critical gap by understanding both the barriers to and opportunities for engaging infectious disease specialists in implementing screening, brief intervention, and referral to treatment in their practices.

Clinical Trials Network (FY 2015 Request: $45.5 million)
NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) comprises 13 research nodes and more than 240 individual community treatment programs in 38 states, plus the District of Columbia and Puerto Rico. The CTN develops and tests the feasibility and effectiveness of promising medications and behavioral treatment approaches for drug abuse and related disorders, such as comorbid mental health disorders and HIV, with diverse patient populations and

community treatment providers. The CTN is currently at the final stage of completing (1) a multi-site study to evaluate the effect of Screening, Brief Intervention, and Referral to Treatment (SBIRT) in emergency departments on substance use and substance-related outcomes, (2) a trial of the safety and effectiveness of Suboxone (buprenorphine) plus Vivitrol (extended-release naltrexone) for the treatment of cocaine addiction in patients also abusing opioids, and (3) a randomized trial evaluating safety and preliminary efficacy of buspirone for relapse-prevention in patients with cocaine addiction. Ongoing studies are evaluating (1) the effect of contingency management on treatment engagement of HIV-infected drug users, (2) comparison of Vivitrol to Suboxone for patients addicted to heroin or other opioids, including prescription pain relievers, (3) N-acetylcysteine for treatment of marijuana addiction, (4) combination therapy with Vivitrol plus Wellbutrin (bupropion) for treatment of methamphetamine addiction, and (5) Vivitrol for HIV positive opioid users in HIV settings.

Intramural Research Program (IRP) (FY 2015 Request: $88.2 million)
The Intramural Research Program performs cutting edge research within a coordinated multidisciplinary framework. The IRP attempts to (1) elucidate the nature of the addictive process; (2) determine the potential use of emerging new therapies for substance abuse, both pharmacological and psychosocial; and (3) establish the long-term consequences of drugs of abuse on systems and organs, with particular emphasis on the brain and its development, maturation, function, and structure.

A prime example of the unique role the IRP plays in furthering substance abuse research is the recently established Designer Drug Research Unit (DDRU), created in response to the worldwide epidemic of synthetic drug abuse. Synthetic drugs are marketed as safe, cheap and legal alternatives to illicit drugs like marijuana, cocaine and ecstasy. However, they can produce serious cardiovascular and neurological side-effects that require emergency medical care and can be fatal. Many popular designer drugs have been rendered illegal by regulatory control, but new replacement analogs are flooding the marketplace at an alarming rate. The NIDA IRP is uniquely poised to respond to this public health crisis, by collecting, analyzing and disseminating current information about the pharmacology and toxicology of newly-emerging designer drugs. The IRP also works collaboratively with NIDA's Extramural Division of Pharmacotherapies and Medical Consequences of Drug Abuse to identify potential targets for addiction medications, an approach that should speed up the progress of selected targets along the NIDA medications development pipeline. In addition, NIDA and NIAAA together have made significant progress at integrating their intramural research programs in substance use, abuse, and addiction, including the appointment of a single Clinical Director for NIAAA and NIDA and the establishment of a joint genetics Intramural Research Program and a common optogenetics lab.

Research Management and Support (RMS) (FY 2015 Request: $62.0 million)
RMS activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. Additionally, the functions of RMS encompass strategic planning, coordination, and evaluation of NIDA's programs, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. NIDA currently oversees more than 1,800 research grants and more than 190 research and development contracts. In addition to the

infrastructure required to support research and training, NIDA also strives to educate the public about drug abuse and addiction and to raise awareness of the science addressing it.

Adolescents are a key target for NIDA's outreach efforts. NIDA created National Drug Facts Week (NDFW), a week-long health observance event held annually at the end of January during which teens and scientists connect at local events to discuss the scientific facts about drug abuse and addiction. In 2013, more than 500 events were held reaching all 50 states. Promotional media activities surrounding the week reached more than 71 million people. Another key audience is health care professionals. In October 2012, the Office of National Drug Control Policy (ONDCP) and NIDA launched two online continuing medical education courses—one focused on safe prescribing for pain, the other on managing patients who abuse prescription opioids—in partnership with Medscape. To date, these courses have been completed nearly 75,000 times for credit. In 2014, NIDA will also publish a new NIDA Principles of Effective Treatment for Adolescents, intended to provide parents, referring clinicians, treatment practitioners, youth, and others with an evidence-based resource to the principles of effective substance abuse treatment for youth.

National Institute of Alcohol Abuse and Alcoholism

The FY 2015 Request is $63.446 million for NIAAA's Underage Drinking activities, which equals to the FY 2014 funding level.

Underage Drinking (FY 2015 Request: $63.446 million)

NIAAA has a strong focus on preventing and reducing underage drinking, recognizing the pervasive use of alcohol among young people, and the association between early initiation of alcohol use and future alcohol problems. In FY 2012, NIAAA released an alcohol screening guide for health care providers to identify alcohol use, and alcohol-use disorders in children and adolescents, and to identify risk for alcohol use, especially for younger children. In FY 2012, NIAAA funded four 5-year studies to evaluate the youth alcohol screening guide, one in a network of emergency departments, one in a juvenile justice setting, one in primary care, and one with youth who have a chronic condition (e.g., asthma or diabetes). In FY 2013, two additional five-year studies were funded to evaluate the guide, one in school settings and another study in primary care. The brief, two-question screener is being assessed in youth ages 9 to 18 as a predictor of alcohol risk, alcohol use, and alcohol problems including alcohol-use disorders, and as an initial screen for other behavioral health problems; for example, other drug use, smoking, or conduct disorder. NIAAA also has a significant investment in underage drinking research including seven ongoing projects that comprise the National Consortium on Alcohol and Neurodevelopment in Adolescence (N-CANDA). Collectively, these projects will follow more than 600 participants through adolescence, using state-of-the-art structural and functional brain imaging and extensive behavioral and clinical assessments to identify the short and long-term effects of alcohol exposure on the developing adolescent brain.

PERFORMANCE

This section on FY 2013 performance is based on agency GPRA documents and other agency information. NIH's GPRA measures are "representative" of Institute contributions to NIH's priorities regarding specific scientific opportunities, identified public health needs, and

Presidential priorities. Such measures, reflecting NIH's broad and balanced research portfolio, are not Institute-specific. Each measure is trans-NIH, encompassing lead and contributory ICs. This approach reflects NIH's commitment to supporting the best possible research and coordination of research efforts across ICs. All performance results reported were achieved in FY 2013.

National Institute on Drug Abuse

NIDA continues to contribute to a number of trans-NIH scientific research outcomes (SROs). One of these, indicative of NIDA's contribution to the prevention of substance abuse and addiction, is SRO-3.5: "By 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies." By identifying genetic factors involved in the various stages of the addiction process, this outcome aids in the development of improved primary (stop drug use before it starts) and secondary (prevent relapse) prevention programs. Please note that NIH is completing SRO-3.5 in FY 2013. In FY 2014, NIH will replace SRO-3.5 with SRO-5.15, which states "By 2018, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance use, abuse, addiction and their consequences in underage populations." Like SRO-3.5, this new measure is indicative of NIDA's efforts to support prevention research related to substance abuse and addiction.

NIDA also contributes to SRO-8.7: "By 2018, identify three effective system interventions generating the implementation, sustainability and ongoing improvement of research-tested interventions across health care systems." By studying treatment implementation, this outcome improves the translation of research into practice.

National Institute on Drug Abuse		
Selected Measures of Performance	**FY 2013 Target**	**FY 2013 Achieved**
» SRO-3.5, by 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies.	Continue to characterize functional genetic variations associated with substance abuse	NIH researchers characterized additional gene variants associated with drug dependence and smoking cessation as well as developed new resources to help interpret the functional significance of identified variants.
» SRO-8.7, by 2018, identify three effective system interventions generating the implementation, sustainability and ongoing improvement of research-tested interventions across health care systems.	Continue ongoing data collection in 2 studies designed to test 3 implementation strategies for incorporating research-supported treatment interventions in the criminal justice system using collaborative implementation protocols.	The CJ-DATS research protocols MATICCE and HIV-STIC completed data collection in FY 2013.

Discussion

Prevention – SRO-3.5

NIDA contributes to NIH's scientific research goal of identifying and characterizing human candidate genes that influence risk for substance use disorders and risk of psychiatric disorders, by funding research to further characterize the functional roles of genetic variations associated with substance abuse.

From 2007 to 2013, multiple genome-wide and targeted association studies have revealed significant associations between genetic variants and substance abuse and addiction. NIDA supported deep sequencing and functional analyses to understand the relationships and mechanisms of how those genetic variants contribute to addiction and its treatment.

Recent work by NIDA-supported researchers has identified new variants associated with opioid addiction. Xie et al. (2013) sequenced 1,520 subjects with co-occurring alcohol, cocaine, and opioid dependence and identified 11 rare variants that showed an association with opioid dependence in an African American sample. Although rare variants were identified in several genes, the bulk of them were identified in DISC1 and GRIN2B genes[1]. This targeted sequencing approach, i.e., repeatedly sequencing a known region, is particularly valuable for substance abuse phenotypes because of what we already know about the genes involved in the metabolism of the substance or major biologic systems that are affected.

[1] Xie P, Kranzler HR, Krystal JH, Farrer LA, Zhao H, Gelernter J. (2013) Deep resequencing of 17 glutamate system genes identifies rare variants in DISC1 and GRIN2B affecting risk of opioid dependence. Addict Biol. [Epub ahead of print]

In other work, NIDA researchers built upon work reported last year on variations in the nicotinic subunit receptor cluster on chromosome 15 that may be associated with response to smoking cessation medications. Bergen et al. evaluated nicotinic receptor subunit polymorphisms in an analysis of 8 separate, but similar, randomized clinical trials. The data show that the abstinence rates at the end of treatment and at 6 months post treatment were influenced by CHRNA5 variants[2]. Another study examined whether these genes predict efficacy of the smoking cessation medications varenicline and bupropion. Continuous abstinence (weeks 9–12) with varenicline treatment was associated with multiple nAChR subunit genes (including CHRNB2, CHRNA5, and CHRNA4); whereas abstinence associated with bupropion treatment was associated with the CYP2B6 gene[3]. Thus, different loci are associated with varenicline vs. bupropion response, suggesting that additional research may identify clinically useful markers to guide treatment decisions.

Another genetic variant of interest, CYP2A6, has been shown to affect how quickly nicotine is metabolized, which in turn influences nicotine use and the efficacy of smoking cessation medications. For example, a recent NIDA-funded study showed that differences in the CYP2A6 gene can predict whether nicotine replacement therapies (nicotine lozenge and/or nicotine patch) will be effective in helping a person quit smoking. The effectiveness of bupropion, a non-nicotine based medication often prescribed to quit smoking, was not affected by differences in this gene[4]. This study adds to previous findings with the CHRNA5 gene, showing that screening for genetic variation may better guide personalized treatments to quit smoking. However, before moving these findings to the clinic, additional data are needed to assess long term outcomes, and generalizability to diverse populations.

Lastly, an important part of functional characterization is using computational approaches to integrate information from a variety of sources. To this end, NIDA has supported several studies to facilitate the discovery and possible functional significance of genetic or chromosomal changes corresponding to disease status. NIDA has supported methods to more robustly identify contributing (or causal) single nucleotide polymorphisms related to addiction[5,6]. (Single nucleotide polymorphisms, or SNPs, are DNA sequence variations that occur when a single nucleotide (A, T, C, or G) in the genome sequence is altered.) In addition, NIDA supported the development of a resource to explore long-range genomic interactions using the WashU Epigenome Browser to gain deeper insights to genomic changes[7].

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[2] Bergen AW, Javitz HS, Krasnow R, Nishita D, Michel M, Conti DV, Liu J, Lee W, Edlund CK, Hall S, Kwok PY, Benowitz NL, Baker TB, Tyndale RF, Lerman C, Swan GE (2013) Nicotinic acetylcholine receptor variation and response to smoking cessation therapies.Pharmacogenet Genomics. 23(2):94-103.

[3] King DP, Paciga S, Pickering E, Benowitz NL. Bierut LJ, Conti DV, Kaprio J, Lerman C, and Park PW. (2012) Smoking Cessation Pharmacogenetics: Analysis of Varenicline and Bupropion in Placebo-Controlled Clinical Trials. Neuropsychopharmacology 37(3): 641–650.

[4] Chen LS, Bloom AJ, Baker TB, Smith SS, Piper ME, Martinez M, Saccone N, Hatsukami D, Goate A, Bierut L. Pharmacotherapy effects on smoking cessation vary with nicotine metabolism gene (CYP2A6). Addiction. Epub ahead of print.

[5] Schwantes-An TH, Culverhouse R, Duan W, Ramnarine S, Rice JP, Saccone NL. (2013) Interpreting joint SNP analysis results: when are two distinct signals really two distinct signals? Genet Epidemiol.37(3):301-9.

[6] Johnson EO, Hancock DB, Levy JL, Gaddis NC, Saccone NL, Bierut LJ, Page GP.(2013) Imputation across genotyping arrays for genome-wide association studies: assessment of bias and a correction strategy. Hum Genet. 132(5):509-22. doi: 10.1007/s00439-013-1266-7.

[7] Zhou X, Lowdon RF, Li D, Lawson HA, Madden PA, Costello JF, Wang T. (2013) Exploring long-range genome interactions using the WashU Epigenome Browser. Nat Methods. 10(5):375-6.

Treatment - SRO-8.7

NIDA also contributes to NIH's scientific research goal of identifying effective implementation strategies that enhance the uptake of research-tested interventions in service systems such as primary care, specialty care, and community practice. NIDA recognizes that despite major strides in treatment research, only limited improvements have occurred in non-research settings. For example, the rates of drug abuse among people involved with the criminal justice system are very high (e.g., 70-85 percent of state inmates) yet few receive treatment while incarcerated (approximately 13 percent), jeopardizing both public health and public safety. To improve drug treatment within the criminal justice system, NIDA continues to support a national multisite research program, the Criminal Justice-Drug Abuse Treatment Studies (CJ –DATS), which tests strategies for how best to implement effective treatment within the criminal justice system.

The CJ-DATS protocol completed data collection in FY 2013; research protocols are described in the FY 2010 target description. Specifically, the ***MATICCE (Medication-Assisted Treatment Implementation in Community Correctional Environments)*** protocol is testing implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies; to increase the number of persons in corrections who are provided medication-assisted treatment (MAT); and improving community corrections agents' knowledge and perceptions about MAT and intent to refer appropriate individuals to community-based MAT services. The interventions to be tested are the Knowledge, Perception, and Information (KPI) intervention and the KPI + organizational linkage (OL) intervention. The KPI intervention consists of professional training for correctional staff on use of medications in addiction treatment. The KPI + OL intervention is intended to improve correctional staff knowledge, perceptions, and capacity for interorganizational relationships to improve referral to, utilization of, and support for medication-assisted treatment appropriate for individuals with substance use disorders.

In FY 2013, all nine research centers completed the active implementation protocol—that is, the strategic planning intervention with the Pharmacotherapy Exchange Council (PEC). To date, in each experimental site, the PEC has completed all assigned protocol activities: an assessment/walkthrough process to identify agency needs, a collaborative strategic planning process to identify key goals for improving offender referrals, the implementation of activities needed to achieve those goals, the production of written summary reports and sustainability plans, and the disengagement from the research teams as planned. All research centers implemented the same study protocol and associated measures.

In FY 2013, the research teams completed end-of-intervention and follow-up data collection at all sites. This included records abstraction from offender case reports at the end of the intervention and at 6 months post-intervention to determine the extent to which offenders are referred to treatment and gains are sustained over time. These data can be compared to referral rates documented at baseline (collected in FY 2011). The second half of FY 2013 was devoted to intensive data cleaning and analysis activities. One paper was submitted for publication[8], and

[8]Belenko S, Hiller M, Visher C, Copenhaver M, O'Connell D, Burdon W, Pankow J, Clarke J, Oser C (2013) Policies and Practices in the Delivery of HIV Services in Correctional Agencies and Facilities: Results From a Multisite Survey. J Correct Health Care, in press.

four main findings papers are being prepared for publication. Research teams presented preliminary findings at several national conferences, including the American Association for the Treatment of Opioid Dependence (AATOD), the Association for Medical Education and Research (AMERSA), and the Academic and Health Policy Conference on Correctional Health. FY 2014 is entirely devoted to data analysis, and reporting of study findings.

HIV Services and Treatment Implementation in Corrections (HIV-STIC) protocol is testing an organizational intervention strategy for more effectively implementing improvements in HIV services for preventing, detecting, and treating HIV in offenders under correctional supervision. The interventions to be tested are an HIV Training for corrections intervention and Local Change Team (LCT) Process Improvement intervention. The HIV training includes basic training on the fundamentals of HIV infection, prevention, testing, and treatment, as well as information about the HIV services continuum and its implications. The process improvement using LCT guides the team through a structured series of quality improvement techniques intended to identify key change targets and to make incremental organizational changes that will improve the quality and coordination of HIV services across correctional and community agencies.

In FY 2013, all nine research centers continued to collect data associated with the active implementation protocol; that is, the HIV training and Local Change Team Intervention. In FY 2013, all sites (experimental and control) have completed the implementation and data collection phases of the study. CJ-DATS investigators submitted three publications to peer-reviewed journal outlets related to the HIV-STIC study during FY 2013. FY 2014 is devoted entirely to data analysis and continued reporting of study findings.

Research Highlights

<u>Long-term effects of universal preventive intervention on prescription drug abuse.</u>
Brief prevention interventions delivered during middle school are effective at reducing students' abuse of prescription drugs throughout adolescence and into young adulthood, according to a new NIDA-funded study. Three randomized controlled trials tested the effects of brief universal interventions (i.e., those targeting all kids) aimed at reducing youth risky behaviors and substance use: (1) the Iowa Strengthening Families Program (ISFP); (2) a modified version of the ISFP called the Strengthening Families Program: For Parents and Youth 10-14 (SFP) coupled with Life Skills Training; and (3) the SFP paired with one of three school-based interventions. All tested interventions were associated with significantly lower prescription opioid abuse and lower lifetime prescription drug abuse overall, and the interventions either were equally or more effective for higher-risk subgroups as for lower-risk groups. This study is the first to examine the long-term effectiveness (6-14 years following the intervention) of brief universal prevention programs on reducing prescription drug abuse throughout adolescence and into young adulthood.

<u>Research suggests that targeted stimulation of the brain's prefrontal cortex is a promising treatment for addiction.</u>
Compulsive drug-taking, despite negative health and social consequences, has been the most difficult challenge in human drug addiction. NIDA researchers used an animal model of cocaine addiction, in which some rats exhibited addictive behavior by pushing levers to get cocaine even when followed by a mild electric shock to the foot. Other rats did not exhibit addictive

responses. The NIDA scientists compared nerve cell firing patterns in both groups of rats by examining cells from the prefrontal cortex. They determined that cocaine produced greater functional brain deficits in the addicted rats. Scientists then used optogenetic techniques on both groups of rats – essentially shining a light onto modified cells to increase or lessen activity in that part of the brain. In the addicted rats, activating the brain cells (thereby removing the deficits) reduced cocaine-seeking. In the non-addicted rats, deactivating the brain cells (thereby creating the deficits) increased compulsive cocaine seeking. This is the first study to show a cause-and-effect relationship between cocaine-induced brain deficits in the prefrontal cortex and compulsive cocaine-seeking.

New breath test may detect recent marijuana use.
Marijuana causes serious impairment in motor skills, judgment, and perception, which are necessary for operating a vehicle safely. In the past, testing drivers for recent marijuana use has not been as simple as testing for alcohol, but preliminary research on the detection of THC (tetrahydroncannabinol) – the main psychoactive chemical in marijuana – in the breath of marijuana smokers may change that. According to NIDA scientists who published their work in September, a new breath test they have developed can, in most cases, detect whether a person used marijuana within the previous ½ hour to 2.5 hours, depending on the frequency of use. This could be a valuable tool for workplace or roadside marijuana testing.

Drug overdose is the leading cause of death in former prisoners.
A new study identifies drug overdose as the leading cause of death in former prisoners, with prescription opioids most commonly involved in these deaths. In addition, women leaving prison had higher mortality rates from opioids, cocaine, and antidepressants than men.

These findings highlight the vulnerability of former prisoners as they transition from prison to the community, suggesting the need for more effective overdose education, monitoring for medical problems, and drug treatment in prison- and community-based mental and health care systems.

National Institute of Alcohol Abuse and Alcoholism
NIAAA continues to contribute to a number of trans-NIH scientific research outcomes (SROs). One which is indicative of NIAAA's contribution to the prevention of substance abuse and addiction is SRO-3.5: "By 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies." By identifying genetic factors involved in the various stages of the addiction process, this outcome aids in the development of improved primary (stop drug use before it starts) and secondary (prevent relapse) prevention programs. In FY 2014, NIH will replace SRO-3.5 with SRO-5.15, which states "By 2018, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance use, abuse, addiction and their consequences in underage populations." Like SRO-3.5, this new measure is indicative of NIAAA's efforts to support prevention research related to underage alcohol abuse and addiction.

In addition NIAAA contributes to SRO-8.7: "By 2018, identify three effective system interventions generating the implementation, sustainability and ongoing improvement of research-tested interventions across health care systems." By focusing on treatment implementation, this outcome improves the translation of research into practice. SRO-8.7 is indicative of NIAAA's efforts to more broadly bring evidence-based treatments for substance addiction to the people who need them.

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2013 Target**	**FY 2013 Achieved**
» SRO-3.5, by 2013, identify and characterize at least two human candidate genes that have been shown to influence risk for substance use disorders and risk for psychiatric disorders using high-risk family, twin, and special population studies.	Complete genome wide association and functional studies and identify potential genomic variants associated with risk for substance use and/or psychiatric disorders.	NIH researchers identified genomic variants that were associated with risk for alcohol dependence.
» SRO-8.7, by 2018, identify three effective system interventions generating the implementation, sustainability and ongoing improvement of research-tested interventions across health care systems.	Refine the underage drinking screening guide based on feedback from primary care providers and develop strategies to encourage widespread adoption of the guide.	NIH supported two additional studies to evaluate its youth alcohol screening guide and developed CME training through Medscape for physicians, nurses and physicians' assistants.

Discussion

Prevention – SRO-3.5

NIH researchers conducted genetic association studies within families in which alcohol dependence is prevalent and identified gene variants associated with alcohol dependence.

For more than two decades NIAAA has supported the Collaborative Studies on Genetics of Alcoholism (COGA), a large-scale national, multi-ethnic, high-risk family study, with the goal of identifying specific genes that can influence a person's likelihood of developing alcohol dependence. This has resulted in a very rich dataset and repository of phenotypic and neurophysiological data, cell lines, and DNA for current and future studies within COGA. A current focus of COGA is the study of adolescents and young adults from these families, to examine genetic effects across development and to understand the environmental factors that modulate genetic risk in this critical age range. Studies on youth from families with a high density of alcohol dependence will enable researchers to examine how genetic variants identified in one generation influence risk in the next generation and how this risk is influenced by various environmental factors. The research will also further explore if exposure to alcohol during key developmental stages causes epigenetic modifications, defined as changes to DNA structure without changes to the DNA sequence that alter gene expression, which may affect the long-term

risk for alcohol dependence and its sequelae. Analyses will also examine the potential association between these epigenetic changes and patterns of alcohol use initiation.

COGA researchers recently completed a genome wide association study (GWAS) and identified gene variants that are potentially associated with risk for alcohol dependence. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), the diagnosis of alcohol dependence is based on endorsement of at least 3 of 7 diagnostic criteria. Rather than focusing on the presence or absence of alcohol dependence as the primary outcome, the investigators in this study used the overall number of alcohol dependence criteria met (from 0 to 7), which some studies have indicated is a good diagnostic tool that may reflect the severity of dependence. This approach expanded the sample population. For example, information on older adolescents who may have begun to experiment with alcohol, but who met only one or two alcohol dependence criteria, was included in the analysis. The GWAS was conducted on more than 2,000 subjects from 118 extended families severely affected by alcohol dependence. The genomic variants that showed the strongest association with the number of alcohol dependence criteria endorsed were located in C15orf53, a gene of unknown function. Other genomic variants in C15orf53 that were previously found to affect risk for bipolar disorder also showed a strong association with alcohol dependence risk in the current study, suggesting shared genetic factors may contribute to both disorders. The investigators attempted to replicate the alcohol dependence findings using data from two other addiction-related studies that did not select participants based on a strong family history of alcohol dependence. In these two studies, the associations were weaker. This suggests that severely affected families may have a concentration of genetic variants that influence risk for alcohol dependence but that has less effect on alcohol dependence in the general population. An alternate explanation is that the small effect size seen in this study may be difficult to replicate in other types of samples, especially those of limited size.[9]

Treatment – SRO-8.7

To encourage use of NIAAA's youth alcohol screening guide, NIAAA developed an online course with Medscape to provide continuing medical education (CME) credits for physicians, nurses, and physician assistants. To date, nearly 8,000 health care providers have been Medscape certified. Previously, NIAAA issued a request for research applications (RFA) to evaluate the youth alcohol screening guide in practice and funded four projects: one in a network of emergency departments, one in a juvenile justice setting, one in primary care, and one with youth who have a chronic condition (e.g., asthma, diabetes). In FY 2013, NIAAA funded two additional five-year studies under the RFA, another one in primary care and one in a school setting. These studies will provide feedback to NIAAA that will facilitate refinement of the guide and help identify settings where use of the guide is appropriate and effective thereby informing strategies for more widespread dissemination.

[9] Wang JC, Foroud T, Hinrichs AL, Le NX, Bertelsen S, Budde JP, Harari O, Koller DL, Wetherill L, Agrawal A, Almasy L, Brooks AI, Bucholz K, Dick D, Hesselbrock V, Johnson EO, Kang S, Kapoor M, Kramer J, Kuperman S, Madden PA, Manz N, Martin NG, McClintick JN, Montgomery GW, Nurnberger JI Jr, Rangaswamy M, Rice J, Schuckit M, Tischfield JA, Whitfield JB, Xuei X, Porjesz B, Heath AC, Edenberg HJ, Bierut LJ, Goate AM. A genome-wide association study of alcohol-dependence symptom counts in extended pedigrees identifies C15orf53. Mol Psychiatry. 2012 Oct 23. doi: 10.1038/mp.2012.143. [Epub ahead of print]

An NIAAA-supported study is being conducted in one of the nation's largest private health care organizations to examine the implementation, effectiveness and cost-effectiveness of SBIRT in reducing adolescent alcohol and other drug use in pediatric care. In this study pediatric practices are randomized to three conditions, i.e., usual care, SBIRT delivered by primary care physicians, and SBIRT delivered by behavioral medicine specialists. SBIRT in this study is based on the CRAFFT screening tool plus referral to treatment. (CRAFFT is a mnemonic acronym based on the first letters of key words in the six screening questions.)

Research Highlights

Study finds missed opportunities for underage alcohol screening.
Although drinking is prevalent among adolescents, doctors often fail to ask and counsel their young patients about drinking. In a random survey of more than 2,500 10th grade students with an average age of 16 years, researchers from NIAAA and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development found that 34 percent reported drinking alcohol in the past month. Twenty-six percent said they had binged, defined as five or more drinks per occasion for males, and four or more for females. While more than 80 percent of 10th graders said they had seen a doctor in the past year, just 54 percent of that group were asked about drinking, and 40 percent were advised about alcohol harms. Furthermore, among students who had been seen by a doctor in the past year and who reported drinking in the past month, only 23 percent said they were advised to reduce or stop drinking. Among the 43 students who said that they were drunk six times or more in the past month and who said they had been asked about their drinking by a doctor, about 30 percent were not advised about drinking risks, and two-thirds were not advised to reduce or stop drinking. The researchers caution that in the survey students were asked about past-month drinking, not what they may have told their physicians about their drinking. Studies have shown that screening and brief interventions by health care providers – asking patients about alcohol use and advising them to reduce risky drinking – can promote significant, lasting reductions in drinking levels and alcohol-related problems among adults. Accumulating evidence supports the use of alcohol screening among adolescents.

Genetic influences on alcohol use across stages of development.
COGA researchers performed a longitudinal analysis to understand how genetic risk for alcohol dependence evolves during the transition from adolescence to young adulthood. There is a substantial body of evidence that has demonstrated genetic associations with alcohol dependence in adults; however, there is limited evidence about genetic associations with alcohol dependence symptoms at much younger ages as well as how genetic risk for problem drinking may change over time. Using a sample of 1,070 adolescents and young adults ages 14-25 from COGA families, the researchers tested whether variants in GABRA2, a gene previously associated with adult alcohol dependence, was associated with risky drinking behavior. In this study, drunkenness during the past 12 months was used as a measure of risky drinking behavior because, at earlier ages, genetic influences may be more evident for patterns of problem drinking than for the classical symptoms used to diagnose alcohol dependence. A significant association was observed between each of the six GABRA2 variants tested and a sudden, substantial increase in drunkenness during the transition from adolescence to young adulthood (age 18 to 19). Although males overall exhibited higher levels of drunkenness in the sample studied, the genetic influence of the GABRA2 variants on the increase during age 18 to 19 was more evident in females. For many individuals, this transitional period is marked by multiple milestones such

as attending college, acquiring greater autonomy and forming new social networks. These findings illustrate that genetic effects differ across development from adolescence to adulthood and gender differences are important in understanding these effects.[10]

Genetic correlates of the age of onset of alcohol use disorders in adolescents and young adults. Research has shown that those who begin to drink at an early age are at greater risk of developing alcohol dependence and early drinking may be influenced by genetic factors. COGA investigators looked at a sample of 2,938 adolescents and young adults ages 12-25 to test if variants in the CHRM2 gene that were previously shown to be associated with adult alcohol dependence could predict the onset of alcohol dependence in adolescents and young adults. The researchers found a significant association with CHRM2 variants and onset of alcohol dependence in adolescents under 16 years of age, including those who also reported ever using an illicit drug. An important difference between this data and the previous adult data was that the CHRM2 variant with the strongest association out of the ones tested was different for the under age 16 group compared to adults.[11]

[10]Dick DM, Cho SB, Latendresse SJ, Aliev F, Nurnberger JI Jr, Edenberg HJ, Schuckit M, Hesselbrock VM, Porjesz B, Bucholz K, Wang JC, Goate A, Kramer JR, Kuperman S. Genetic influences on alcohol use across stages of development: GABRA2 and longitudinal trajectories of drunkenness from adolescence to young adulthood. Addict Biol. 2013 May 20. doi: 10.1111/adb.12066. [Epub ahead of print]

[11] Chorlian DB, Rangaswamy M, Manz N, Wang JC, Dick D, Almasy L, Bauer L, Bucholz K, Foroud T, Hesselbrock V, Kang SJ, Kramer J, Kuperman S, Nurnberger J Jr, Rice J, Schuckit M, Tischfield J, Edenberg HJ, Goate A, Bierut L, Porjesz B. Genetic and neurophysiological correlates of the age of onset of alcohol use disorders in adolescents and young adults. Behav Genet. 2013 Sep;43(5):386-401. doi: 10.1007/s10519-013-9604-z. Epub 2013 Aug 21.PMID: 23963516 [PubMed - in process]