As the Director of the National Institutes of Health (NIH), I am pleased to present the Congressional Justification of the NIH fiscal year (FY) 2016 budget request. This budget request for $31.311 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. In addition, it highlights research investments that will increase understanding of underlying disease causes and spur development of diagnostics, treatments, and preventive approaches to improve health. It will enable NIH to recruit and support a talented and diverse workforce to bring new insights to our understanding of biology and 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 process to determine how best to distribute its resources among a careful balance of short- and long-term basic and applied research activities and the scientific infrastructure needed to accomplish them. The strength of this approach is evidenced by the extraordinary number of innovative discoveries in biomedical science produced through NIH-funded research. In FY 2016, NIH will continue to focus on striking a balanced research portfolio that enhances health while reducing illness and disability. This includes unraveling life's mysteries through basic research, translating discovery into health, harnessing data and technology to improve health, and preparing a diverse and talented biomedical research workforce.

The processes we have in place allow for the necessary flexibility to capitalize on scientific opportunities, respond immediately to urgent public health needs, and build the evidence base for the future of health care. This flexibility was apparent when responding to the global Ebola crisis in 2014, centered on an outbreak in West Africa. In our response, NIH quickly provided support for researchers to track the virus' spread as well as to pursue new prevention and treatment strategies to combat the disease.

Furthermore, NIH continues to build foundations to encourage revolutionary improvements to the prevention and treatment of disease and disability. We are capitalizing on recent advances in technology and our understanding of individual genetic variability to discover more precise means for delivering more tailored health care. Called precision medicine, this area holds the promise to develop new approaches to address disease prevention, novel therapeutics, and medical devices.

Overall, the FY 2016 budget request will enable NIH to continue its investments in groundbreaking research, scientific workforce training, and technologies of the future. NIH will retain the flexibility to prioritize research that reduces illness, increases disease prevention, and responds to emerging public health needs.

I look forward to discussing the FY 2016 budget request and NIH's plans for the future.

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

TABLE OF CONTENTS

EXECUTIVE SUMMARY

OVERALL APPROPRIATIONS

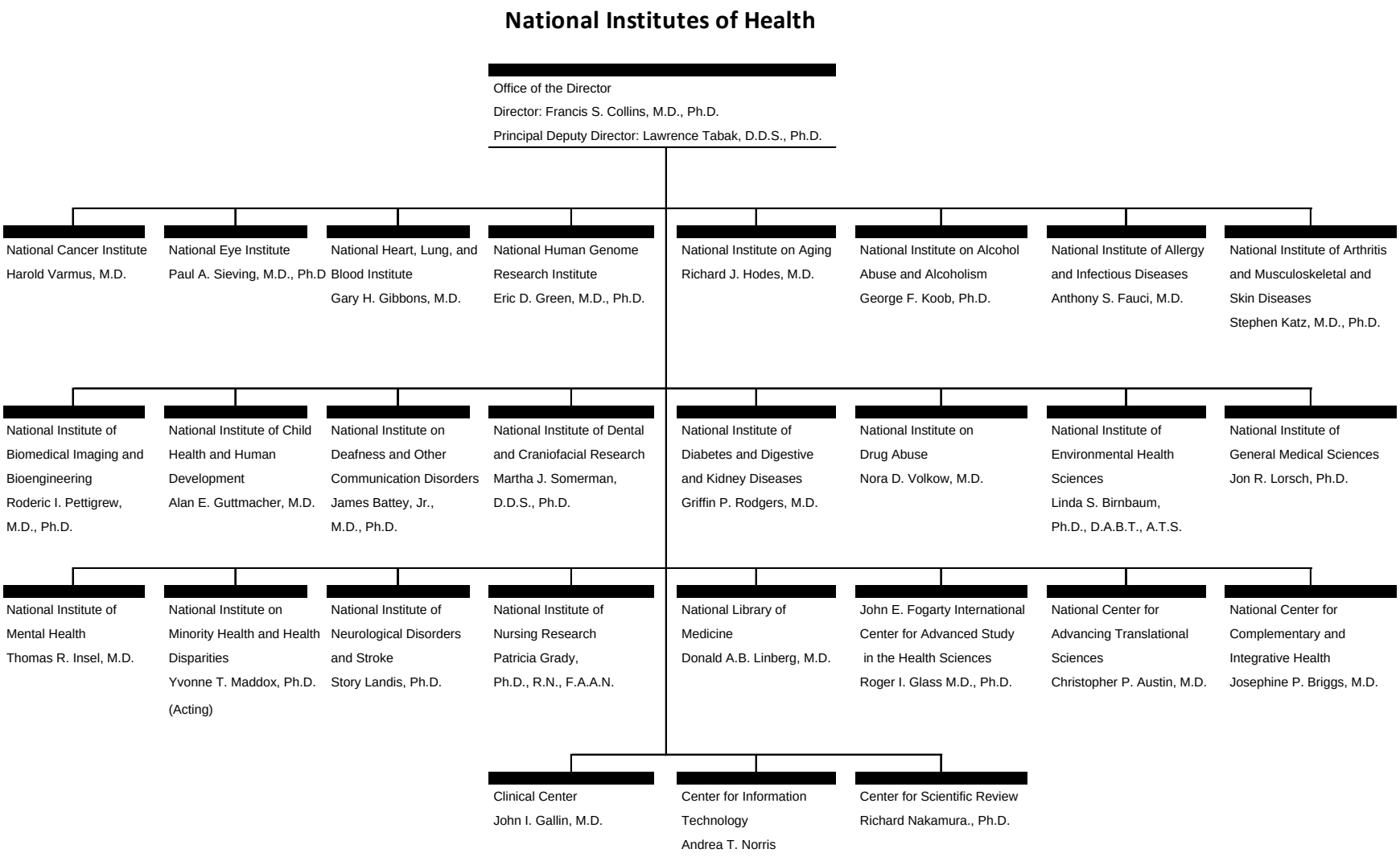
SUPPLEMENTARY TABLES

COMMON FUND

OFFICE OF AIDS RESEARCH

DRUG CONTROL PROGRAMS

ORGANIZATION CHART



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 toward designing new approaches for preventing, diagnosing, and treating disease and disability; and ensure that these new approaches are available to all.

As the Nation's medical research agency and the largest source of funding for biomedical and behavioral research in the world, NIH plays a unique role in turning basic scientific discovery into tangibles that improve health. A significant and enduring investment by NIH in basic research today guarantees the breakthroughs in health care tomorrow. To realize such breakthroughs, NIH also invests in research that will translate these basic findings into the delivery of effective health care. Novel research methods stimulated by technological advances, including the generation of complex data sets, are facilitating extraordinary opportunities to address previously unanswerable questions about biology, behavior, and medicine. This robust research enterprise depends upon NIH's continued innovation, as it seeks to recruit and retain the Nation's brightest minds into successful scientific careers. With continued support, NIH 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.

ALL PURPOSE TABLE

(Dollars in Thousands)	FY 2014 Actual	FY 2015 Enacted[1]	FY 2016 President's Budget	FY 2016 Request +/- FY 2015 Enacted
Total, NIH Program Level	**$30,070,062**	**$30,311,349**	**$31,311,349**	**$1,000,000**
Less funds allocated from different sources:				
Mandatory Type 1 Diabetes Research	-139,200	-150,000	-150,000	0
PHS Program Evaluation	-8,200	-715,000	-847,489	-132,489
Total, NIH Discretionary Budget Authority	**$29,922,662**	**$29,446,349**	**$30,313,860**	**$867,511**
Interior Budget Authority	-77,349	-77,349	-77,349	0
Total, NIH Labor/HHS Budget Authority	**$29,845,313**	**$29,369,000**	**$30,236,511**	**$867,511**
Number of Competing RPGs	*9,168*	*9,076*	*10,303*	*1,227*
Total Number of RPGs	*34,332*	*34,206*	*35,447*	*1,241*
FTEs	*18,048*	*18,150*	*18,150*	*0*

[1] Excludes Ebola-related funding.

OVERVIEW OF BUDGET REQUEST

For Fiscal Year (FY) 2016, NIH requests a total program level of $31.3 billion which is $1.0 billion above the FY 2015 Enacted level. This request reflects both the President's and the Secretary's commitment to improving the health of all Americans and to maintaining the country's leadership in the biomedical sciences. For more than a hundred years, NIH has advanced the understanding of human health and disease through its investments in biomedical research, and the results of this research have helped improve health, lengthen life, and reduce illness and disability for many generations. NIH's work produces important secondary benefits to the Nation as well, including job creation, regional and global economic activity, international competitiveness, intellectual property, and commercializable products, to name a few. For example, a recent health and financial analysis of one clinical trial undertaken through NIH's Women's Health Initiative has demonstrated the robust return that NIH provides to the American public. The study estimated that one postmenopausal hormone therapy trial resulted in long-term financial and health outcomes worth $37.1 billion in net economic gain, a return of approximately $140 on every dollar invested in the trial.[1]

In order to maintain excellence, NIH must continue to fund a strong, diverse portfolio of biomedical research, flexible enough to capitalize on scientific opportunities and to respond to urgent public health needs as they arise. For example, the recent Ebola epidemic in West Africa allowed NIH to demonstrate this flexibility in responding to a public health emergency. Numerous NIH-funded scientists utilized established biomedical research infrastructure to identify the source and track the spread of the epidemic using advanced genetic sequencing technologies, develop multiple promising vaccine candidates in tandem with the private sector, perform Phase I vaccine safety and efficacy clinical trials, and take steps to perform advanced clinical vaccine testing in an afflicted country.

To strike this delicate balance in its biomedical research portfolio, in FY 2016, NIH will focus on the following priority themes:

1. Unraveling Life's Mysteries through Basic Research
2. Translating Discovery into Health
3. Harnessing Data and Technology to Improve Health
4. Preparing a Diverse and Talented Biomedical Research Workforce

By pursuing these priorities, NIH will continue to take on the critical scientific challenges that must be faced to improve health, reduce disability, and drive the engines of discovery and innovation. Often these challenges are ones that NIH is uniquely poised to pursue because of the Agency's expertise, resources, and deep commitment to health and the public good.

Theme 1: Unraveling Life's Mysteries through Basic Research

As the largest funder of basic biomedical science in the world, NIH has a long tradition of supporting transformative basic science breakthroughs. Basic, foundational research is a major driver of progress across the biological and behavioral sciences – advances in fields such as genomics, proteomics, stem cells, the microbiome, imaging, and other technologies have

[1] See: http://www.ncbi.nlm.nih.gov/pubmed/24798522

transformed our understanding of how life works, have led to the discovery of more than a thousand risk factors for disease, and have yielded inestimable benefits to public health. Basic research often paves the way for unexpected scientific advances and unanticipated health applications. For example, NIH-funded scientists built upon the finding that a single light-sensitive protein controls the movement of green algae toward sunlight to develop optogenetics, a game-changing technique that allows scientists to selectively turn neurons in the brain on or off merely by exposing them to light. Similarly, early advances in the field of nanoscience laid the groundwork for developing innovative, body-friendly nanotools to help scientists build synthetic biological devices, such as miniature, implantable pumps for drug delivery, or tiny sensors to scan for the presence of infectious agents that could spell trouble for the body. By supporting a broad basic research portfolio, NIH helps to forge the biomedical breakthroughs of tomorrow. Below are a few examples of basic science areas of particular promise for FY 2016.

Single Cell Biology

Individual cells within the same tissues, organs, or parts of the body may differ dramatically, and these differences can have important consequences for the overall health of an organism. Yet, because of technical limitations, most *in vivo* biological research until very recently has been focused on tissue segments involving millions of cells. New technologies and experimental approaches now hold out the promise of analyzing and targeting single cells within large, complex biological environments.

Through a focus on single cell biology, NIH is challenging scientists to address significant hurdles that currently exist in measuring the given "state" of a cell, defining normal cell-to-cell variation, detecting the impact of different environmental changes, and understanding how collections of diverse cell types function together as part of a larger whole. Through the Common Fund's Single Cell Analysis Program, NIH funded nearly $8 million in research in 2014 to unravel the workings of single cells.

Not only can scientists now study individual cells in their native state, NIH-funded scientists recently developed a powerful new tool called CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), which allows precise targeting of genes for deletion, addition, activation, or suppression – with such specificity that it amounts to performing genetic microsurgery, potentially at the level of a single cell. The method harnesses a protein that is involved in a bacteria's adaptive immune response that works through precise targeting of DNA. CRISPR has been used to alter genes in cells from bacteria, mice, and humans, and even to engineer monkeys with specific mutations that could serve as more accurate models of human disease. By cultivating the next generation of technologies for single cell analysis, NIH-funded scientists are primed to uncover fundamental biological principles and ultimately improve the detection and treatment of disease.

Advanced Cellular Imaging

Advanced imaging techniques allow scientists to peer into the human body with pinpoint accuracy and reveal the inner workings of living tissue in extraordinary detail. Several recent advances in imaging technology by NIH-funded researchers are making it easier to produce high-resolution, three-dimensional molecular movies and even capture nanoscale chemical reactions occurring in real time. Three cellular imaging techniques – X-ray free-electron lasers, electron cryomicroscopy (cryo-EM), and light microscopy – illustrate how quickly these imaging technologies are evolving. For one, newly developed X-ray free-electron lasers are a major

innovation that produces X-ray pulses faster and more powerfully than ever before. With the capability of accelerating particles to nearly the speed of light, free-electron X-ray lasers are strong enough to pierce through steel and fast enough to capture strobe-like images of molecular motions. Second, innovations in cryo-EM are using faster, more efficient cameras to obtain pictures of biological complexes at near-atomic resolution. Lastly, continual refinements in light microscopy have made it possible, for example, to conduct cellular-level brain imaging in freely moving animals and to stage high-throughput, automated screening of drug effects in animal models of disease.

With all of this progress, a number of technical hurdles remain, such as boosting the power and brightness of free-electron lasers, further increasing image resolution, and developing novel approaches to analyzing the deluge of data that advanced cellular imaging tools produce. In FY 2016, NIH will continue to fund scientists who are pushing the boundaries of biological imaging capabilities.

The 4D Nucleome

While great strides have been made in mapping the human genome and understanding the many factors that control gene expression in health and disease, our increasing knowledge continues to lead to big questions and new scientific opportunities. From research on the human genome came a refined appreciation for the epigenome, the host of non-DNA elements that control gene expression and can be strongly influenced by the environment. Likewise, there is a growing appreciation for the critical role of the spatial, three-dimensional organization of the nucleus, the physical structure within each cell that houses most DNA. Recent basic research suggests that the spatial distribution of DNA and other DNA-interacting molecules within the nucleus is far from random and changes dynamically over time, adding yet a fourth dimension to an already complex picture – thus, an emerging line of research focuses on unraveling the 4D nucleome. Harmful alterations in the organization of the nucleome are associated with rare genetic disorders as well as certain cancers and premature aging syndromes.

Beginning in FY 2015 and ramping up in FY 2016, the 4D Nucleome Initiative will support basic research into the architecture of the nucleus, how it changes over time, as well as its relationship to gene expression, cellular health, and disease states. NIH-funded scientists also will explore the role of epigenetic modifications in the four dimensions of DNA organization inside the nucleus, as well as develop tools and databases to encourage collaboration and accelerate the study of the 4D Nucleome. In the long term, the primary goal of this program is to understand how the physical structure of genetic material within the nucleus influences the function of the genome in order to better understand complex disease pathways, which could yield important clues to developing a new generation of diagnostics and therapeutics.

The BRAIN Initiative

The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative was launched by the President on April 2, 2013, as a bold new effort to revolutionize our understanding of the human brain. The complexity of the human brain was once thought to be beyond our understanding – the brain comprises nearly 100 billion nerve cells that make an astounding 100 trillion connections. Through this initiative, NIH and its partners are driving the development and use of innovative technologies to produce a clearer, dynamic picture of the brain that can show, for the first time, how individual cells and complex neural circuits interact in both time and space.

This multi-agency initiative leverages the unique strengths of NIH, the Defense Advanced Research Projects Agency (DARPA), the National Science Foundation (NSF), the Food and Drug Administration (FDA), and the Intelligence Advanced Research Projects Activity (IARPA), as well as private funders. Given the ambitious goals of the BRAIN Initiative, success will require ideas from the best scientists and engineers across many diverse disciplines. NIH's funding priorities have been guided by a high-level working group of the Advisory Committee to the NIH - the NIH BRAIN working group - which was composed of expert scientists around the country. Its planning process sought input broadly from the scientific community, patient advocates, and the general public.

The NIH BRAIN working group first released an interim report in December 2013, which informed and guided funding priorities for FY 2014 BRAIN initiative funding. On June 5, 2014, the working group released its much-anticipated recommendations for a strategy encompassing FY 2016 – FY 2025. The plan includes a bold agenda for progress, including specific goals, milestones, and deliverables. Nine specific objectives are geared toward developing novel, cutting-edge tools to image and control neural activity in order to better understand the architecture and function of the brain. Ultimately, the technologies developed under the BRAIN Initiative may help reveal the underlying pathology in a vast array of brain disorders and provide new therapeutic avenues to treat, cure, and even prevent neurological and psychiatric conditions, such as Alzheimer's disease, autism, depression, schizophrenia, and addiction.

On September 30, 2014, NIH awarded the initial round of grants for the BRAIN Initiative, totaling $46 million. These grants included six funding initiatives, covering a wide array of topics from better understanding the cells and circuits of the brain to developing better tools to measure and manipulate their activity to the next generation of non-invasive human functional imaging. These funds represent only the initial investment in these tools and approaches for understanding the brain. To accomplish the initiative's ambitious goals, and to allow the United States to lead the world in this cutting-edge area of science, the working group recommended a significant ramp-up in funding. The request includes $135 million an increase of $70 million for BRAIN in FY 2016.

Theme 2: Translating Discovery into Health

NIH is heavily invested in translating its basic scientific discoveries into fruitful health applications. Translational sciences turn observations in the laboratory and clinic into effective interventions that improve the health of individuals and the public, from diagnostics and therapeutics to medical procedures, behavioral changes, and disease prevention strategies. All of NIH's 27 Institutes and Centers are involved in this effort; below are a few examples of areas of special opportunity in FY 2016.

Precision Medicine

Historically, medical practitioners have had to make recommendations about disease prevention and treatment based largely on the expected response of an average patient. However, recent advances in technology, along with decreasing costs of DNA sequencing, have developed a compelling and innovative approach to medicine by using individual variability. This emerging practice is known as precision medicine.

Precision medicine allows treatments to be tailored to the individual characteristics of each patient. To accomplish this, scientists and physicians must understand human variability and

identify individuals who differ in the susceptibility to a particular disease, in the trajectory of a disease, or in response to a specific treatment. In this way, specific preventive or therapeutic interventions can be adapted for each patient–avoiding needless treatment and expense for those who will not benefit.

NIH understands the importance of treating disease at an individual level, and has made precision medicine a priority. In FY 2014, two cancer precision medicine clinical trials commenced, both capitalizing on the infrastructure of the National Clinical Trials Network supported by the National Cancer Institute (NCI). The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials, or ALCHEMIST, will identify early-stage lung cancer patients with tumors that have certain uncommon genetic changes. Patients will receive one of two supplemental treatments specifically targeted to these genetic alterations to determine if the drugs prevent cancer recurrence and prolong life. The Lung Cancer Master Protocol (Lung-MAP) trial for patients with advanced squamous cell lung cancer will test four experimental drugs. This trial is a unique public-private collaboration between NIH, non-profit organizations, and pharmaceutical companies. Patients are assigned to a particular drug (or "arm" of the trial) based on the results of a genetic screen for cancer-related genes. Unlike previous clinical trials, Lung-MAP tests patients for many biomarkers simultaneously to assess compatibility with several different treatment options. This innovative trial design could be pivotal as advances in precision medicine make this type of treatment possible.

As part of the President's multi-agency Precision Medicine Initiative, NIH plans to spend $200 million on precision medicine in FY 2016. The battle against cancer has been leading the way in precision medicine for many years. To capitalize on these successes, the FY 2016 request proposes $70 million to expand current cancer genomics research to initiate new studies of how a tumor's DNA can be used to predict and treat tumor cells that develop resistance to a therapy, apply new non-invasive methods to track response to therapy, and explore the efficacy of new combinations of cancer drugs targeted to specific tumor mutations. In addition, to harness the full potential of precision medicine across many diseases, NIH proposes $130 million to launch a national research cohort of a million or more individuals, primarily those who have already participated in clinical research studies, who volunteer to share their genetic information in the context of other health data over time. This information will be linked to their electronic health records, while ensuring privacy protections are in place. A database of this scale will lay the foundation for a wealth of new research studies which promises to lead to new prevention strategies, and novel therapeutics and medical devices. It will also help improve how drugs are prescribed, allowing a more optimum choice of the right drug at the right dose for the right person.

Ebola Virus Research and Vaccine Development

Ebola virus disease can cause severe illness and death in humans and other primates. In early 2014, the first cases of a new Ebola virus outbreak were reported in West Africa - now the largest and most complex Ebola outbreak in history.

Alongside colleagues throughout the Federal Government, NIH sought to understand how this virus emerged as well as how to reduce or eliminate the threat it presents to public health at home and abroad. NIH-funded researchers used advanced genomic sequencing technologies to identify the single point of transmission from an animal host to a human in the current outbreak.

The findings highlight how NIH basic science investments can be deployed rapidly to assist in tracing origins of newly emerging microbial threats.

As there are yet no approved drugs or vaccines to fight Ebola virus disease, prompt diagnosis and aggressive supportive care can improve patient survival. Due in part to its support for Ebola vaccine development since 2001, NIH started several Phase I clinical trials of investigational, human Ebola vaccines in the fall of 2014. These trials used vaccines created from public private partnerships with pharmaceutical companies. Initial results are promising, and NIH will learn from the results and improve these vaccines with the goal of initiating more advanced, Phase II/III clinical trials of investigational Ebola vaccines in affected countries.

NIH will continue to provide input and direction for key policy decisions related to the Ebola response. For example, clinical researchers are developing a master protocol for comparing robust supportive care with experimental therapies in patients infected with Ebola at designated treatment facilities in the United States. Furthermore, the additional $238 million provided in emergency appropriations in FY 2015 will help NIH to perform the in-country advanced clinical trials necessary to combat the disease along with accelerating the identification and evaluation of new pre-clinical prevention and treatment approaches for Ebola.

Stem Cells

Recent research has demonstrated that stem cells have the remarkable potential to develop into many different cell types in the body. In many bodily tissues, stem cells serve as a kind of internal repair system, dividing extensively to replenish other cells as long as the person or animal is alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. A recently developed research technique, which garnered the 2012 Nobel Prize in Physiology or Medicine, now makes it possible to create a new type of stem cell called an induced pluripotent stem (iPS) cell in the laboratory – iPS cells 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 turned into a wide variety of cell types, including liver cells, neurons, cardiac cells, and blood cells. NIH-funded scientists are studying iPS cells and other types of stem cells, not only to understand better cell function and disease pathways, but also to develop therapies for a variety of diseases and disabilities, including Parkinson's disease, amyotrophic lateral sclerosis (ALS), spinal cord injuries, heart disease, diabetes, and arthritis. For example, an NIH intramural scientist is pursuing preclinical efficacy and safety studies with retinal pigment epithelium tissue, developed from a patient's own skin cells using iPS technology, to treat age-related macular degeneration, a leading cause of blindness in the elderly. Another condition for which stem cell treatment has shown particular promise is sickle cell disease (SCD). SCD is a serious inheritable disorder in which the body makes sickle-, or crescent-shaped red blood cells, which, unlike their normal counterparts, are stiff and sticky and tend to block blood flow in limbs and organs. Blocked blood flow can cause pain and lead to organ damage, and also can raise the risk for serious infection. Currently, hematopoietic stem cells, or blood-producing stem cells found in bone marrow and peripheral blood, are used to treat SCD, but transplant rejection is a major risk, and the treatments can have severe consequences and life-threatening complications. The advent of iPS cell technology has raised the possibility of a novel therapeutic strategy – skin cells from a patient could be programmed to become pluripotent and self-renewing, and then engineered (perhaps using new genome editing techniques) to correct the sickle mutation. Differentiating those cells into hematopoietic stem

cells and infusing them back to the individual could provide a potential cure, with no risk of transplant rejection.

Influenza Vaccines

Influenza, or the flu, is a respiratory infection that can be caused by several different viral strains. Most people who become infected feel better within a week, although they may have a lingering cough and tire easily for a while longer. An estimated 5 to 20 percent of Americans are infected during each flu season, which typically lasts from October to March. For the elderly, newborns, pregnant women, immunocompromised persons, and people with certain chronic illnesses, the flu and its complications can be life-threatening, and each year more than 200,000 people are hospitalized. Although most recover from the illness, between 3,000 and 49,000 Americans die as a result of the flu and its complications every year.

Currently, receiving the seasonal vaccine is the best way to prevent the flu, despite the scientific 'guess work' used to select the strain most likely to emerge each year and the risk of new emerging strains with pandemic potential. Using cutting-edge knowledge of immunology, genomics, and structural biology, NIH-funded scientists are making significant progress in the development of a universal influenza vaccine. A universal vaccine could confer decades-long protection from any influenza strain, be it seasonal or a possible pandemic strain (e.g., H1N1, H5N1, and H7N9). Strain detection and vaccine development are complicated and time consuming activities, so NIH works closely with its Federal Government agency partners, including the Centers for Disease Control and Prevention (CDC) and FDA, as well as experts in academia, industry, and foreign governments. In FY 2016, the Biological Advanced Research and Development Authority (BARDA) and NIH will work with HHS to prioritize activities that best align with the ongoing HHS strategy to develop a universal influenza vaccine. An increase of $20 million is requested in FY 2016 to accelerate this research.

HIV Vaccine and Cure Research

An estimated 36 million people have died from AIDS since the first cases were reported in 1981, while more than 35 million people worldwide are now thought to be infected with HIV. NIH's long-term support of HIV/AIDS research has resulted in more than 30 FDA-approved therapeutics and various strategies to reduce the spread of the virus. Moreover, a top priority for NIH remains developing a safe, effective, and affordable HIV vaccine. Such a vaccine would need to be used in combination with other prevention, treatment, and behavioral approaches in order to end the AIDS pandemic.

NIH-funded researchers are designing and evaluating safe and effective vaccine candidates to prevent HIV infection. NIH is currently investigating the reasons for the modest efficacy (31 percent protection) of the HIV vaccine candidates used in the RV-144 clinical trial conducted in Thailand in 2009 and will seek to achieve significantly better results with future vaccine candidates. NIH has funded two new promising HIV vaccine initiatives and also is exploring in clinical trials whether or not passively transferred neutralizing antibodies can protect against HIV infection. Marking the 25th annual World AIDS Day, President Obama announced in December 2013 that the NIH will redirect $100 million of AIDS research funds to expand research towards a cure for HIV. Many promising recent basic and translational research advances targeting viral reservoirs, pockets of cells or tissues where HIV can hide and evade the host immune system, suggest that a complete cure, or at least lifelong remission, of HIV infection may be possible. The majority of the funds will support basic HIV research, along with advanced studies focused

on improving animal models, drug development, preclinical testing of antiretroviral compounds, and clinical evaluation of therapeutic vaccines and other immune enhancers. Research into prevention strategies, understanding how certain factors affect treatment and/or disease progression, and the increased incidence of co-morbidities in patients on lifelong treatment also will be addressed. The increased attention given to HIV cure research will add to previous successes to treat HIV and continue the NIH's effort to move towards an AIDS-free generation. An increase of $100 million is requested in FY 2016 to expand NIH's HIV/AIDS research.

Antimicrobial Resistance (AMR)

Public health surveillance has documented an alarming increase in AMR in pathogenic bacteria, especially those that cause hospital-acquired infections, tuberculosis, and gonorrhea. AMR is an inevitable outcome of the evolutionary principle that organisms will mutate to escape lethal selective pressure; by acquiring genetic mutations and reproducing rapidly, some bacteria can evade destruction by drugs. As long as antibiotics are used to kill bacteria, resistance will continue to emerge. This process is exacerbated by the overuse and misuse of existing antimicrobial drugs. More than 70 percent of bacteria that cause healthcare-associated infections in the United States are resistant to at least one commonly used antibiotic, and bacteria resistant to all known antibiotics are appearing with increasing frequency. According to CDC, antibiotic resistance in the United States costs an estimated $20 billion per year in excess health care costs, $35 million in other societal costs, and more than 8 million additional days that people spend in the hospital. Each year in the United States, more than 2 million people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a result of these infections, and many more die from other conditions that were complicated by an antibiotic-resistant infection.

Recognizing the growing public health threat of AMR, the Administration has issued its *National Strategy for Combating Antibiotic-Resistant Bacteria.* In accordance with this Strategy, NIH (in concert with CDC, FDA, and the U.S. Department of Agriculture), is engaging in a number of key efforts designed to reverse the trend of illness and death due to increasing bacterial resistance to antimicrobials and address a major emerging threat to public health. First, to help ensure that antibiotics are prescribed appropriately, NIH will spur the development of new, rapid diagnostics. In collaboration with BARDA, FDA, and CDC, a competition is being designed for the development of a rapid diagnostic test that will be of great clinical and public health utility in combating AMR. A prize or prizes totaling at least $20 million will be announced by the end of FY 2016 and later awarded to the winning group(s) with the goal of incentivizing the development of a transformative diagnostic. Second, NIH will develop a national database of genomic sequence data on all reported human infections with antibiotic-resistant microorganisms. This will provide a critically needed resource for surveillance, epidemiology, and basic research into the mechanisms underlying the emergence of antimicrobial resistance. Third, NIH will launch a large-scale effort to characterize and understand drug resistance, focusing on the changes in host/pathogen molecular interactions that occur as bacteria develop resistance in response to antibiotic treatment. This knowledge is essential to developing accurate diagnostics and new therapeutic approaches. Fourth, NIH will expand its Antibiotic Resistance Leadership Group to create a rapid response clinical trial network that is ready to test new antibiotics on individuals infected with highly resistant strains. The request includes $461 million an increase of $100 million in FY 2016 to support the National Strategy.

Accelerating Medicines Partnership (AMP)

While technological advances have produced a wealth of data on the biological causes of disease, translating these discoveries into treatments has been far more difficult. Choosing the wrong drug target often results in failures in the drug development process, costing time, money, and, ultimately, lives. Developing a new drug typically takes well over a decade and has a failure rate of more than 95 percent, with many failures occurring late in the process. As a result, each success costs more than $1 billion.

The good news is that researchers have identified more than a thousand new potential targets for drug therapy in the last five years, offering an encouraging path forward. AMP seeks to spur entirely new approaches to the development of the next generation of drugs in order to increase the number of new diagnostics and therapies for patients while also reducing the time and cost of their development. It is essential for the pharmaceutical enterprise to pinpoint the right biological targets much earlier in the drug development process. AMP represents an unprecedented partnership between NIH, the Foundation for the NIH, FDA, 10 pharmaceutical companies, and a number of non-profit organizations. By focusing on optimizing how disease targets are identified and validated for drug design, AMP aims to help drug researchers choose the right targets faster. The AMP partnership plans to invest close to $230 million over five years, with total costs shared equally between NIH and the industry partners. The first AMP projects are focused on Alzheimer's Disease, Type 2 Diabetes, and the autoimmune disorders of lupus and rheumatoid arthritis. As this model gains in scientific strength, it is expected that other companies may join, and other disorders can be proposed for inclusion. A critical component of this collaboration is that industry partners have agreed to make AMP data and analyses publicly accessible to the broader biomedical research community. In FY 2016, NIH expects to spend $23 million for this initiative, the same level as in FY 2015.

Alzheimer's Disease (AD)

AD is a progressive, and, at present, irreversible brain disease that slowly destroys memory and thinking skills, and eventually even the ability to carry out the simplest tasks of daily living. The disease progresses in three stages, from a preclinical stage where no symptoms are present, to a middle stage of mild cognitive impairment, and ending with a final stage of Alzheimer's dementia. The time from diagnosis to death varies by person; it can be as little as three or four years if the person is older than 80 when diagnosed, but it can be as long as 10 or more years if the person is younger. Estimates vary, but experts suggest that as many as five million Americans age 65 and older have AD. Although treatment can help manage symptoms in some people, currently there is no cure for this devastating disease.

NIH supports a comprehensive program of research on AD. NIH focuses on basic neuroscience research, epidemiologic studies to identify risk and protective factors for cognitive impairment and AD, genetic studies to identify risk and protective genes, clinical studies to identify biomarkers for early disease diagnosis and for disease progression, and testing of interventions to prevent and treat the disease. NIH works with many partners and its coordination efforts have been facilitated greatly by the recent launch of the International Alzheimer's Disease Research Portfolio (IADRP), a publicly available database to capture the full spectrum of current AD research investments and resources, both in the United States and internationally. Developed by the National Institute on Aging (NIA) in collaboration with the Alzheimer's Association, the

IADRP will enable public and private funders of AD research to coordinate research planning, leverage resources, avoid duplication of funding efforts, and identify new opportunities in promising areas. Along with NIA, more than 20 NIH Institutes and Centers and a number of other Federal and non-Federal agencies from around the world contribute to the database.

Turning the tide on AD is a domestic and international priority. NIH's long-term planning efforts are one component of HHS's National Plan to Address Alzheimer's Disease, updated in April 2014 with input from numerous experts in aging and AD from Federal, State, private and non-profit organizations, as well as caregivers and people with the disease. As the lead agency in implementing Goal #1 of the National Plan to Prevent and Effectively Treat Alzheimer's Disease by 2025, NIH has adopted milestones to achieve a number of research objectives. NIH and many other Federal agencies have been active participants in Global Action Against Dementia (GAAD), a G7 effort launched in December 2013. In February 2015, NIH will host a research summit on Alzheimer's Disease that will include international participation and presentations, followed by a half-day meeting focused on G7 research tracking and collaborations. NIH's ability to identify new research opportunities and track research progress will be aided by these international collaborative efforts, including the IADRP. NIH will continue to work with its many partners until an effective treatment or cure can be found for this terrible disease. The request includes an additional $51 million for AD research in FY 2016, for an estimated total of $638 million.

Theme 3: Harnessing Data and Technology to Improve Health

Rapid expansion of technological capabilities has opened new horizons for biomedical research. Biomedical science continues to generate immense and complex datasets that present challenges for data creation, storage, and analysis, but also extraordinary opportunities to answer questions about biology, behavior, and medicine that previously were unanswerable. Innovative research methods stimulated by technological advances are facilitating the development of new strategies to diagnose, prevent, and treat a host of diseases. Technology also facilitates the integration of previously disparate fields, such as biology and electronics, enabling NIH to cultivate new lines of medical research and practice.

Utilizing Technology to Combat Cancer

Due in large part to advances in rapid sequencing technology, NIH-supported research is paving the way for individualized precision medicine in cancer treatment. Until recently, cancer treatments were limited to surgery, radiation, and chemotherapy, which all carry risks and typically lack the precision to attack only cancerous cells. New research strategies in which the therapy is optimized for a particular person based on key characteristics of their specific cancer cells holds the promise of a transformation in cancer treatment. NIH laid the foundation for these therapies by supporting The Cancer Genome Atlas (TCGA) to provide a comprehensive genomic analysis of many cancer types, and the continued success of the TCGA is due in large part to advances in rapid sequencing technology. Data generation and analysis for TCGA projects will continue into FY 2016, and the foundational datasets gathered through this research, as well as important methodological advances, will be applied to improve patient outcomes in the future.

For example, TCGA and other basic research has informed the development of targeted therapies for cancer, which use drugs to inhibit specific proteins on cancer cells that are linked to the behavior of those cells. In one instance, NIH-supported researchers developed a new technology

to analyze proteins on the surface of cancer cells that could be ideal targets for treatment. The new technology uses a highly sensitive method that requires just a few of a patient's cells and could eventually lead to determining which treatment will be most effective for each patient.

Named *Science* magazine's 2013 Breakthrough of the Year, another promising and rapidly developing treatment option driven by technology is cancer immunotherapy, which directs the patient's own immune system to attack cancer cells. In one approach, certain types of immune cells, called T-cells, are collected from cancer patients and engineered to produce special proteins on their surface. When these engineered T-cells are infused back into patients, they have the power to seek and destroy cancer cells. Initial trials of this type of therapy have been very successful, opening up new opportunities for cancer precision medicine.

Applying the Microbiome

Using powerful genomic sequencing technologies, researchers in 2012 reported the "healthy" human microbiome, which includes trillions of microbes (bacteria, fungi, and viruses). In 2007, NIH launched the Human Microbiome Project (HMP) with the goal of increasing understanding of the microbes living in and on the human body and their role in health and disease. More recent efforts focus on characterizing how the microbiome is related to specific diseases, creating the first integrated dataset of biological properties from both the microbiome and the host. These research efforts have generated more than 14 terabytes of sequencing data, highlighting not only the need for continued investment in this growing area of science, but also the need to augment NIH investments in data coordination and management systems.

By using these high-throughput multi-omics analyses (the collective characterization and quantification of different groups of biological molecules) to study the human microbiome, researchers are unearthing connections to diseases that could have a major impact on public health. For example, a study in mice that have features of autism spectrum disorder pointed to a possible link between the gut microbiome and autism. In this research, an oral treatment targeted at altering the microbiome resulted in improved behavior in the mice. A number of studies also have examined the role of the microbiome in obesity, uncovering a link between an increase in the amount of one kind of bacteria and a decrease in certain other bacteria depending on the subject's weight. The microbiomes of people with Type 2 Diabetes have distinct features as well, and additional research may uncover whether these differences play a role in causing the disease or if the differences are a result of the disorder, as well as lead to potential treatments.

Big Data to Knowledge

The computational needs for maintaining, securing, and processing large-scale digital datasets go far beyond the capabilities of individual investigators and even individual institutions. Biomedical Big Data can come in many forms – through the use of sophisticated technologies such as high-definition brain imaging, next-generation gene sequencing, and mHealth (mobile health) applications to track and improve health behaviors with the support of mobile devices, just to name a few. NIH is playing a major role in coordinating access to and analysis of the many types of biological and behavioral Big Data generated by biomedical scientists. To this end, NIH developed the Big Data to Knowledge (BD2K) Initiative in 2012 with the goal of establishing systems and expertise that enable optimal use of Big Data in biomedical science. NIH announced an initial investment of $32 million in BD2K awards in FY 2014, with projections for a total investment of over $600 million through 2020, pending available funds.

With the recent appointment of an Associate Director for Data Science at NIH, the BD2K program will expand in FY 2016 (by $19.5 million) and beyond.

The BD2K Initiative focuses on developing innovative and transformative approaches as well as tools to make Big Data and data science a prominent component of biomedical research. Funding opportunities concentrate on four major areas: enabling data utilization by the development of a Data Commons; analysis methods and software; enhancing training; and centers of excellence. For example, in FY 2016, NIH will support awards to train scientists at all career levels in Big Data science as well as for developing courses for skills development and open educational resources.

Bioelectronic Medicine

Advances in a range of biomedical science disciplines and coincident technology development have opened the door for NIH to support a new, high-risk, goal-driven research area. Bioelectronic medicine describes a newly forged field of "electroceuticals" that combines electronics and biology to treat a wide variety of diseases and conditions, by harnessing the powerful influence of the peripheral nervous system. In bioelectronic medicine, nano-scale electronic devices are connected to groups of nerve fibers, and then electrical impulses are used to stimulate the peripheral nerves throughout the body, the autonomic nervous system that regulates involuntary functions, and the enteric nervous system that controls the gastrointestinal system. With scientific advances that are mapping disease-specific neural circuits, bioelectronic medicine has the potential to control the function of physiologic systems and treat such conditions as hypertension and chronic pain.

NIH's new bioelectronic medicine program – Stimulating Peripheral Activity to Relieve Conditions (SPARC) – will develop proof-of-concept for an entirely new class of neural control devices that have the potential to restore health to organs and to ameliorate biological deficiencies. Using Other Transaction Authority (OTA), NIH will fund high-risk, discrete goal-focused, and milestone-driven research supported through the NIH Common Fund, as well as numerous Institutes and Centers. Basic research funded by NIH, including efforts to map the human brain, as well as to identify how particular nerves in the body relate to specific diseases, will inform significantly the field of bioelectronic medicine. Additionally, the program will support projects to establish precise and effective methods for administering electrical impulses to the nervous system. NIH anticipates spending $30 million for this program in FY 2016.

National Patient-Centered Clinical Research Network

Although mountains of health information are generated every day as part of routine visits between a patient and a physician, our capacity to study and compare clinical outcomes data from multiple clinical centers has been extremely limited. To address this issue, the non-governmental Patient-Centered Outcomes Research Institute (PCORI) launched PCORnet: the National Patient-Centered Clinical Research Network. PCORnet is a network of 11 clinical data research networks and 18 patient-powered research networks representing more than 100 million covered lives. PCORnet will harness the data from these networks to support clinical research in a large, highly representative network and provide much-needed answers to pressing clinical questions quickly and inexpensively. This research will be fully funded by PCORI .

In FY 2016, NIH will continue to expand its investments in observational and interventional comparative effectiveness trials using research networks such as the PCORnet platform.

PCORnet is unique in that it brings together patients, care providers, and health systems in partnerships to embed research into routine clinical practice in order to find out what treatments and health care practices work in the real world.

Theme 4: Preparing a Diverse and Talented Biomedical Research Workforce

Biomedical research can only advance and eventually produce the cures and treatments that improve human health if there is a workforce of diverse, well-trained, and highly creative people who can conduct this important work. NIH cultivates the human capital needed to fulfill its mission by providing training grants and fellowships to graduate students and postdoctoral researchers. In addition, NIH has taken steps to enhance diversity in the workforce and to prepare young scientists for careers in this dynamic field by equipping them with training that crosses sectors and disciplines.

Attracting and retaining creative individuals in the biomedical research workforce requires a stable funding environment and opportunities for career growth. Without this, young scientists and even well-established investigators may become discouraged and pursue other career options.

Supporting Innovative Researchers and Transformative Research

The pace of biomedical research is often perceived as slow, as researchers advance knowledge in an incremental process. The High-Risk High-Reward (HRHR) program, funded initially through the Common Fund, seeks to complement this process by supporting innovative investigators whose research goals are potentially transformative and would represent a significant leap ahead in scientific knowledge. Within this program, Pioneer Research Awards are available to investigators at any career stage; New Innovator Awards are for early-stage investigators; Transformative Research Awards are open to scientists at any career stage and are the only HRHR awards open to teams of investigators; and Early Independence Awards are open to exceptional junior scientists within one year of completing their terminal research degree or clinical residency. The HRHR program has led to hundreds of high-impact scientific discoveries and publications, patents, and enhanced collaboration. An evaluation of the Pioneer Award program has found that research conducted by Pioneer awardees is highly innovative, with a greater impact than traditional R01 grantees.[2]

In addition to those HRHR activities managed within or in collaboration with the NIH Common Fund, a number of NIH Institutes and Centers are now introducing similar programs of their own. The National Institute on Drug Abuse (NIDA) adopted the Pioneer award mechanism for its Avant Garde Award Program for HIV/AIDS Research, which supports highly creative scientists who propose novel approaches to HIV/AIDS research that also is relevant to drug abuse. The Biobehavioral Research Awards for Innovative New Scientists (BRAINS) funded by the National Institute of Mental Health (NIMH) helps exceptional, early-career scientists launch innovative research programs that have the potential to transform mental health research. The National Institute of Environmental Health Sciences (NIEHS) offers the Outstanding New Environmental Scientist (ONES) Award to inventive new scientists who are committed to advancing knowledge about the effect of environmental exposure on health. Other Institutes

[2] See: http://commonfund.nih.gov/pioneer/evaluations

adopting their own HRHR awards include the National Institute of General Medical Sciences, which plans to pilot the Maximizing Investigators' Research Award in FY 2016.

Strengthening the Biomedical Research Workforce

Technological advances and a new understanding of the vast complexity of biological and behavioral systems are moving biomedical research toward increasingly multidisciplinary work, in which individuals from many different sectors collaborate to ensure scientific progress. Non-traditional career paths also have become increasingly common as funding for academic research positions has leveled off and even declined. Given the changing research environment and unpredictable future, it is vital to equip young scientists with a range of skills and experiences, as was recommended by the Advisory Committee to the Director (ACD) Biomedical Research Workforce Working Group.[3] NIH has responded to these changes by giving graduate students and postdoctoral scientists exposure to career options in many different sectors. The Broadening Experiences in Scientific Training (BEST) Awards allow trainees to supplement their academic experience with training in industry, non-profits, government, policy, science communication, and other settings within the biomedical research enterprise. NIH created a Division of Biomedical Research Workforce Programs, including a Labor Economist charged with modeling the workforce, expanding NIH's understanding of workforce dynamics through economic analysis, and managing the Biomedical Research and Development Price Index. Using better analysis of the biomedical workforce and evaluation of NIH policies will enable NIH to align its programs and policies with workforce needs.

NIH also is committed to training physician-scientists, whose ability to bridge the lab and clinic is vital to translating scientific discoveries to clinical practices. However, the number of physician-scientists entering the biomedical research workforce has declined in recent years. To address this trend, NIH asked ACD to recommend actions NIH should take to support a sustainable and diverse physician-scientist workforce. ACD formed the Physician-Scientist Workforce Working Group to deliberate this topic, and the group studied the impact of various NIH training programs and considered major challenges that hinder entry into the workforce. In June 2014, the Working Group reported their recommendations for strengthening the training of physician-scientists, especially for those early in the pipeline.[4] Some of these recommendations included developing tools to better track training outcomes and career choices, grant mechanisms and award processes to support aspiring physician-scientists, pilot programs to test approaches to improve and/or shorten research training, and increasing efforts to diversify the physician-scientist workforce.

Enhancing Diversity

The biomedical workforce of the future should reflect the diversity of the public it serves. NIH strongly supports the goal of enhancing the diversity of the biomedical workforce and is taking steps to strengthen it by attracting the most talented individuals from all groups, with particular attention to the recruitment of individuals from economically disadvantaged and underrepresented backgrounds, as identified by the National Science Foundation.[5] To that end,

---

[3] See: http://acd.od.nih.gov/Biomedical_research_wgreport.pdf
[4] See http://acd.od.nih.gov/reports/PSW_Report_ACD_06042014.pdf
[5] See http://www.nsf.gov/statistics/wmpd/2013/pdf/nsf13304_digest.pdf

NIH has taken a number of steps to foster diversity, including the appointment of a new NIH Chief Officer for Scientific Workforce Diversity in March 2014.

The Enhancing the Diversity of the NIH-Funded Workforce Program was established by NIH to provide individuals from underrepresented backgrounds with the support and tools necessary to participate in the biomedical workforce. Awarded in FY 2014, the program consists of three integrated initiatives that support a consortium of more than 50 investigators and partnering institutions who work together to develop and test new ways of training and mentoring young scientists. The Building Infrastructure Leading to Diversity (BUILD) Initiative is a set of experimental training awards designed to learn how to attract a diverse array of students into the training pipeline and to encourage their persistence to become future NIH-supported researchers. The 10 BUILD awardees will work with multiple partnering institutions with high concentrations of students from disadvantaged backgrounds to implement transformative, broad-based approaches to the training and mentoring of students to undertake biomedical research. The National Research Mentoring Network (NRMN) was established to increase access to high-quality research mentorship and networking opportunities by establishing a nationwide, interconnected set of skilled mentors linked to mentees from a variety of scientific disciplines, develop best practices for mentoring, provide training for mentors, as well as professional opportunities for mentees. Finally, the Coordinating and Evaluation Center (CEC) will rigorously evaluate BUILD and NRMN to determine the efficacy of new approaches being tested, facilitate the development of consortium-wide hallmarks of success, and serve as the focal point for dissemination of successful training and mentoring strategies.

NIH will continue to develop new ways to engage and sustain the interest of young scientists from underrepresented backgrounds with the goal of attracting them to careers in biomedical research. Achieving this goal will require NIH to share the strategies and tools young scientists need throughout the training process and at all career stages. Evaluations from CEC will provide the evidence for determining which approaches are successful, and results will be disseminated widely so that others can adopt these approaches.

Conclusion

The Nation's investment in NIH, which funds biomedical researchers in every State across the country, has led to countless advances in the sciences of human health and disease. Each year, approximately 83 percent of NIH's budget is awarded through more than 60,000 research and research training grants to the Nation's finest institutions, small businesses, and scientists. Scientific and technological breakthroughs generated by NIH-supported research have fueled many of this country's gains in health and longevity. A child born today can look forward to an average lifespan of about 79 years - nearly three decades longer than a baby born in 1900.[6] Much of the recent improvement in death rates and life expectancy can be attributed to reductions in death rates from major causes of death, such as heart disease, cancer, stroke, and chronic lower respiratory diseases. Over the past 60 years, deaths from heart disease have fallen by more than 70 percent. Cancer death rates have been dropping more than 1 percent annually for the past 15 years (annual decline of 1.8 percent for men and 1.4 percent for women), resulting in life

[6] Xu J, Kochanek KD, Murphy SL, and Arias E. NCHS Data Brief: Mortality in the United States, 2012. Centers for Disease Control and Prevention. Oct 2014; Number 168. http://www.cdc.gov/nchs/data/databriefs/db168.htm

expectancy gains that are estimated to have saved the United States trillions of dollars.[7, 8] Likewise, HIV/AIDS treatments have extended lives greatly, and emerging strategies are enabling us to envision the first AIDS-free generation since this virus emerged more than 30 years ago. Federal Government funding contributed to the development of 48 percent of all drugs approved by the FDA and 65 percent of drugs that have received priority review between 1988 and 2005.[9]

NIH-funded research not only improves the health of Americans but also provides significant benefits to the U.S. economy. NIH research helps to reduce health care spending by producing better, more cost-effective therapies and preventive strategies. For example, a universal flu vaccine could reduce incidence and deaths significantly and potentially reduce the estimated $87.1 billion in annual medical costs, loss of lives, and lost productivity. NIH research also creates jobs and generates economic growth for the country. According to a report from United for Medical Research, in 2012, NIH funding supported more than 400,000 jobs across all 50 States and the District of Columbia.[10] In another independent analysis, Battelle's *2014 Global R&D Funding Forecast* states, "large research initiatives like the Human Genome Project or the War on Cancer...have high rates of social and economic return over the long term."[11] Battelle's *The Impact of Genomics on the U.S. Economy* describes the staggering economic return from genomics research: the $3.8 billion initial investment by the United States in the Human Genome Project (HGP) plus the additional $8.5 billion in HGP-related research and support has resulted in nearly $1 trillion of economic growth. Amazingly, the cost of this Federal funding, according to Battelle, is only $2 per year for each U.S. resident.[12]

Recognizing the large role that biomedical science plays in innovation and economic growth, many countries around the world have increased substantially their investment in biomedical science. While global investment in medical research is to be welcomed, as the largest funder of biomedical research in the world, NIH must continue to be a leader in this enterprise, supporting transformative basic, translational, and clinical research that will advance the health of the Nation, and preparing a highly creative and productive workforce to meet the major biomedical challenges of today and tomorrow.

---

[7] Jemal A, Simard EP, Dorell C, et al. Annual Report to the Nation on the Status of Cancer, 1975–2009, Featuring the Burden and Trends in HPV-Associated Cancers and HPV Vaccination Coverage Levels. *J Natl Cancer Inst*. 2013 Feb 6;105(3):175-201.

[8] Murphy KM and Topel RH. The Value of Health and Longevity. *Journal of Political Economy*, 2006, 114(5).

[9] Sampat BN, Lichtenberg FR. What are the respective roles of the public and private sectors in pharmaceutical innovation? *Health Affairs*. 2011; 30:332-339.

[10] United for Medical Research. 2012. *NIH's Role in Sustaining the U.S. Economy*. http://www.unitedformedicalresearch.com/wp-content/uploads/2012/07/NIHs-Role-in-Sustaining-the-US-Economy-2011.pdf

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

[12] Battelle. 2013. *The Impact of Genomics on the U.S. Economy*. http://web.ornl.gov/sci/techresources/Human_Genome/publicat/2013BattelleReportImpact-of-Genomics-on-the-US-Economy.pdf

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	FY 2015 Enacted[1]	FY 2016 President's Budget	FY 2016 +/- FY 2015
Research Project Grants	$16,332.639	$17,205.659	5.3%
Competing Average Cost (in thousands)	$457.312	$460.696	0.7%
Number of Competing Awards (whole number)	9,076	10,303	13.5%
Estimated Competing RPG Success Rate (absolute rate)	17.2%	19.3%	12.4%
Research Centers	$2,699.292	$2,636.643	-2.3%
Other Research	$1,844.207	$1,882.049	2.1%
Training	$762.071	$785.483	3.1%
Research & Development Contracts	$2,898.740	$2,895.964	-0.1%
Intramural Research	$3,425.860	$3,520.574	2.8%
Research Management and Support	$1,560.897	$1,580.442	1.3%
Common Fund (non-add)	*$545.639*	*$565.639*	*3.7%*
Buildings & Facilities Appropriation	$128.863	$128.863	0.0%
Other Mechanisms[2]	$658.779	$675.673	2.6%
Total, Program Level[3]	**$30,311.349**	**$31,311.349**	3.3%

[1] Excludes Ebola-related funding.

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

[3] 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 Program Evaluation Financing.

OVERVIEW OF PERFORMANCE

The 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 2016 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. NIH 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. In this request, NIH is proposing 45 new measures to replace those that ended or will be ending soon. The development of the new measures was coordinated by the Office of the Director (OD), which identified gaps in the NIH's performance measure portfolio, and sought input from all 27 Institutes and Centers (ICs), as well as key offices within OD, to fill these gaps. A multi-level review process, supported by two trans-NIH committees, was used to develop, refine, and select measures that best align with the Agency's performance priorities. All of NIH's 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 2016, in support of Objective A (Accelerate the process of scientific discovery to improve health) under Goal 2, NIH will support promising biomedical research and human capital investment with the goals of: 1) identifying two molecular-targeted therapies for disorders of the immune system in

children, and 2) providing research training for predoctoral trainees and fellows as well as postdoctoral fellows to promote greater retention and long-term success in research careers.

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 ICs and OD. 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 and seven standing Working Groups.[13,14] 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.

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.

[13] 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.

[14] The seven standing working groups are: Extramural Activities, Diversity, Facilities, Management and Budget, Scientific Data Council, Administrative Data Council, and Clinical Center Governing Board.

BUDGET BY HHS STRATEGIC OBJECTIVE

(Dollars in Millions)	FY 2014 Actual	FY 2015 Enacted[1]	FY 2016 President's Budget
1.Strengthen Health Care			
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 and preventive care, linked with community prevention services			
1.D Reduce the growth of health care costs while promoting high-value, effective care			
1.E Ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations			
1.F Improve health care and population health through meaningful use of health information technology			
2. Advance Scientific Knowledge and Innovation	**29,934**	**30,174**	**31,166**
2.A Accelerate the process of scientific discovery to improve health	29,934	30,174	31,166
2.B Foster and apply innovative solutions to health, public health, and human services challenges			
2.C Advance the regulatory sciences to enhance food safety, improve medical product development, and support tobacco regulation			
2.D Increase our understanding of what works in public health and human services practice			
2.E Improve laboratory, surveillance, and epidemiology capacity			
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 and 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 across the life span			
3.E Reduce the occurrence of infectious diseases			
3.F Protect Americans' health and safety during emergencies, and foster resilience to withstand and respond to emergencies			
4. Ensure Efficiency, Transparency, Accountability, and Effectiveness of HHS Programs	**136**	**137**	**145**
4.A Strengthen program integrity and responsible stewardship by reducing improper payments, fighting fraud, and integrating financial, performance, and risk management			
4.B Enhance access to and use of data to improve HHS programs and to support improvements in the health and well-being of the American people			
4.C Invest in the HHS workforce to help meet America's health and human services needs			
4.D Improve HHS environmental, energy, and economic performance to promote sustainability	136	137	145
TOTAL	**30,070**	**30,311**	**31,311**

[1] Excludes Ebola-related funding.

BUDGET MECHANISM TABLE

(Dollars in Thousands) [1, 2]	FY 2014 Actual		FY 2015 Enacted[7]		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	23,504	$10,785,361	23,433	$11,294,016	23,303	$11,524,971	-130	$230,955
Administrative Supplements	*(1,588)*	208,245	*(1,479)*	172,045	*(1,420)*	168,834	*(-59)*	-3,212
Competing:								
Renewal	1,897	1,297,091	2,049	1,062,346	2,264	1,143,837	215	81,491
New	7,223	3,167,751	6,987	3,078,440	7,996	3,592,077	1,009	513,637
Supplements	48	14,318	40	9,781	43	10,641	3	859
Subtotal, Competing	9,168	$4,479,160	9,076	$4,150,567	10,303	$4,746,555	1,227	$595,988
Subtotal, RPGs	32,672	$15,472,767	32,509	$15,616,627	33,606	$16,440,359	1,097	$823,732
SBIR/STTR	1,660	695,480	1,697	716,012	1,841	765,300	144	49,288
Research Project Grants	34,332	$16,168,247	34,206	$16,332,639	35,447	$17,205,659	1,241	$873,020
Research Centers:								
Specialized/Comprehensive	1,117	$1,958,143	1,130	$1,929,147	1,171	$1,894,298	41	-$34,849
Clinical Research	60	413,671	60	416,824	60	411,742		-5,082
Biotechnology	93	167,045	94	165,694	99	152,972	5	-12,722
Comparative Medicine	51	129,353	52	131,500	49	122,254	-3	-9,246
Research Centers in Minority Institutions	22	55,067	21	56,127	20	55,377	-1	-750
Research Centers	1,343	$2,723,280	1,357	$2,699,292	1,399	$2,636,643	42	-$62,650
Other Research:								
Research Careers	3,624	$611,866	3,632	$614,794	3,648	$619,919	16	$5,125
Cancer Education	96	32,932	96	32,932	96	32,738		-195
Cooperative Clinical Research	394	474,587	385	468,828	386	503,987	1	35,160
Biomedical Research Support	111	67,391	105	64,579	105	64,579		
Minority Biomedical Research Support	287	104,470	283	103,115	282	102,920	-1	-195
Other	1,722	555,627	1,689	559,959	2,010	557,907	321	-2,053
Other Research	6,234	$1,846,873	6,190	$1,844,207	6,527	$1,882,049	337	$37,842
Total Research Grants	41,909	$20,738,399	41,753	$20,876,138	43,373	$21,724,351	1,620	$848,213
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,058	$136,141	3,105	$140,036	3,234	$146,846	129	$6,810
Institutional Awards	12,258	602,287	12,426	622,034	12,501	638,636	75	16,602
Total Research Training	15,316	$738,429	15,531	$762,071	15,735	$785,483	204	$23,412
Research & Develop. Contracts	2,211	$2,990,140	2,078	$2,898,740	2,095	$2,895,964	17	-$2,777
(SBIR/STTR) (non-add)	*(115)*	*(65,426)*	*(129)*	*(73,771)*	*(132)*	*(78,580)*	*(3)*	*(4,810)*
Intramural Research	7,060	$3,384,285	7,087	$3,425,860	7,080	$3,520,574	-7	$94,714
Res. Management & Support	5,574	1,527,790	5,624	1,560,897	5,631	1,580,442	7	19,544
(SBIR Administrative) (non-add)	*(3)*	*(3,687)*	*(30)*	*(4,054)*	*(0)*	*(0)*	*(-30)*	*(-4,054)*
Office of the Director - Appropriation [3]		*(1,303,014)*		*(1,413,734)*		*(1,442,628)*		*(28,894)*
Office of the Director - Other		477,354		573,430		582,324		8,894
ORIP/SEPA (non-add) [3]		*(294,486)*		*(294,665)*		*(294,665)*		*(0)*
Common Fund (non-add) [3]		*(531,174)*		*(545,639)*		*(565,639)*		*(20,000)*
Buildings and Facilities[4]		136,316		136,863		144,863		8,000
Appropriation		*(128,663)*		*(128,863)*		*(128,863)*		*(0)*
Type 1 Diabetes[5]		-139,200		-150,000		-150,000		0
Program Evaluation Financing[6]		-8,200		-715,000		-847,489		-132,489
Subtotal, Labor/HHS Budget Authority		**$29,845,313**		**$29,369,000**		**$30,236,511**		**$867,511**
Interior Appropriation for Superfund Research		77,349		77,349		77,349		0
Total, NIH Discretionary Budget Authority		**$29,922,662**		**$29,446,349**		**$30,313,860**		**$867,511**
Type 1 Diabetes		139,200		150,000		150,000		0
Total, NIH Budget Authority		**$30,061,862**		**$29,596,349**		**$30,463,860**		**$867,511**
Program Evaluation Financing		8,200		715,000		847,489		132,489
Total, Program Level		**$30,070,062**		**$30,311,349**		**$31,311,349**		**$1,000,000**

[1] All Subtotal and Total numbers may not add due to rounding.
[2] All numbers in italics and brackets are non-add.
[3] Number of grants and dollars for the Common Fund, ORIP and SEPA components of OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriations also is noted as a non-add since the remaining funds are accounted
[4] Includes B&F appropriation and funds for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
[5] 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.
[6] Number of grants and dollars for Program Evaluation Financing are distributed by mechanism above; therefore, the amount is deducted to provide subtotals only for the Labor/HHS Budget Authority.
[7] Excludes Ebola related funding.

APPROPRIATIONS LANGUAGE

NATIONAL CANCER INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cancer, [$4,950,396,000] *$5,098,479,000*, of which up to [$8,000,000]*$16,000,000* 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, [$2,997,870,000]*$3,071,906,000*.

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, [$399,886,000]*$406,746,000*.

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, [$1,749,681,000]*$1,788,133,000*.

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, [$1,605,205,000]*$1,660,375,000*.

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]*$4,614,779,000*.

[For an additional amount for National Institute of Allergy and Infectious Diseases to prevent, prepare for, and respond to Ebola domestically and internationally, including expenses related to carrying out section 301 and title IV of the PHS Act, $238,000,000, to remain available until September 30, 2016: Provided, That such amount is designated by the Congress as an emergency requirement pursuant to section 251(b)(2)(A)(i) of the Balanced Budget and Emergency Deficit Control Act of 1985.]

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to general medical sciences, [$2,371,476,000]*$2,433,780,000*, of which [$715,000,000]*$847,489,000* shall be from funds available under section 241 of the PHS Act[: 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, [$1,286,571,000]*$1,318,061,000*.

NATIONAL EYE INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, [$684,191,000]*$695,154,000*.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to environmental health sciences, [$667,502,000]*$681,782,000*.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For necessary expenses for 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.

NATIONAL INSTITUTE ON AGING

For carrying out section 301 and title IV of the PHS Act with respect to aging, [$1,199,468,000]*$1,267,078,000*.

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, [$521,665,000]*$533,232,000*.

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, [$405,302,000]*$416,241,000*.

NATIONAL INSTITUTE OF NURSING RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to nursing research, [$140,953,000]*$144,515,000*.

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, [$447,408,000]*$459,833,000*.

NATIONAL INSTITUTE ON DRUG ABUSE

For carrying out section 301 and title IV of the PHS Act with respect to drug abuse, [$1,028,614,000]*$1,047,397,000*.

NATIONAL INSTITUTE OF MENTAL HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to mental health, [$1,463,036,000]*$1,489,417,000*.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to human genome research, [$499,356,000]*$515,491,000*.

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, [$330,192,000]*$337,314,000*.

NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to complementary and integrative health, [$124,681,000]*$127,521,000*[: Provided, That these funds may be used to support the transition enacted in section 224 of this Act].

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, [$269,154,000]*$281,549,000*.

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), [$67,786,000]*$69,505,000*.

NATIONAL LIBRARY OF MEDICINE

For carrying out section 301 and title IV of the PHS Act with respect to health information communications, [$336,939,000]*$394,090,000*: Provided, That of the amounts available for improvement of information systems, $4,000,000 shall be available until September 30, [2016]*2017*: Provided further, That in fiscal year [2015]*2016*, 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").

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, [$635,230,000]*$660,131,000*: Provided, That up to [$9,835,000]*$25,835,000* 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
(INCLUDING TRANSFER OF FUNDS)

For carrying out the responsibilities of the Office of the Director, NIH, [$1,401,134,000]*$1,430,028,000*, of which up to [$25,000,000]*$30,000,000* may 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 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) or research related to the Study's goals and mission, and any funds in excess of the estimated need shall be transferred to and merged with the accounts for the various Institutes and Centers to support activity related to the goals and objectives of the NCS: Provided further, That NIH shall submit a spend plan on the NCS's next phase to the Committees on Appropriations of the House of Representatives and the Senate not later than 90 days after the date of enactment of this Act]: Provided further, That

[$533,039,000]*$553,039,000* shall be available for the Common Fund established under section 402A(c)(l) 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 NIH shall contract with the National Academy of Sciences for a Blue Ribbon Commission on Scientific Literacy and Standing: Provided further, That NIH shall submit to Congress an NIH-wide 5-year scientific strategic plan as outlined in sections 402(b)(3) and 402(b)(4) of the PHS Act no later than 1 year after enactment of this 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*.

In addition to other funds appropriated for the Common Fund established under section 402A(c) of the PHS Act, $12,600,000 is appropriated to the Common Fund from the 10-year Pediatric Research Initiative Fund described in section 9008 of title 26, United States Code, for the purpose of carrying out section 402(b)(7)(B)(ii) of the PHS Act (relating to pediatric research), as authorized in the Gabriella Miller Kids First Research Act.

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, [$128,863,000]*$128,863,000*, to remain available [through September 30, 2019]*until expended*.

DIVISION G, TITLE II
GENERAL PROVISIONS

[SEC. 224. Title IV of the PHS Act is amended by: (1) Striking “National Center for Complementary and Alternative Medicine” in each place it appears and replacing it with “National Center for Complementary and Integrative Health”; (2) Striking “alternative medicine” in each place it appears and replacing it with “integrative health”; (3) Striking all references to “alternative and complementary medical treatment” or “complementary and alternative treatment” in each place either appears and inserting “complementary and integra1tive health”; (4) Striking references to “alternative medical treatment” in each place it appears and inserting “integrative health treatment”; and (5) Striking section 485D(c) and inserting: “(c) In carrying out subsection (a), the Director of the Center shall, as appropriate, study the integration of new and non-traditional approaches to health care treatment and consumption, including but not limited to nontraditional treatment, diagnostic and prevention systems, modalities, and disciplines.”.]

SEC. 225. In addition to amounts provided herein, payments made for research organisms or substances, authorized under section 301(a) of the PHS Act, shall be retained and credited to the appropriations accounts of the Institutes and Centers of the NIH making the substance or organism available under section 301(a). Amounts credited to the account under this authority shall be available for obligation through September 30, [2016] *2017*.

[SEC. 230. Hereafter, for each fiscal year through fiscal year 2025, the Director of the National Institutes of Health shall prepare and submit directly to the President for review and transmittal to Congress, after reasonable opportunity for comment, but without change, by the Secretary of Health and Human Services and the Advisory Council on Alzheimer's Research, Care, and Services, an annual budget estimate (including an estimate of the number and type of personnel needs for the Institutes) for the initiatives of the National Institutes of Health pursuant to the National Alzheimer's Plan, as required under section 2(d)(2) of Public Law 111–375.]

[SEC. 230. Hereafter, for each fiscal year through fiscal year 2025, the Director of the National Institutes of Health shall prepare and submit directly to the President for review and transmittal to Congress, after reasonable opportunity for comment, but without change, by the Secretary of Health and Human Services and the Advisory Council on Alzheimer's Research, Care, and Services, an annual budget estimate (including an estimate of the number and type of personnel needs for the Institutes) for the initiatives of the National Institutes of Health pursuant to the National Alzheimer's Plan, as required under section 2(d)(2) of Public Law 111–375.]

LANGUAGE ANALYSIS

Language Provision	Explanation/Justification
NATIONAL CANCER INSTITUTE For carrying out section 301 and title IV of the PHS Act with respect to cancer, $4,950,396,000, of which up to [$8,000,000]*$16,000,000* may be used for facilities repairs and improvements at the National Cancer Institute—Frederick Federally Funded Research and Development Center (FFRDC) in Frederick, Maryland. (Department of Health and Human Services Appropriations Act, 2015.)	NIH requests the NCI repairs and improvement cap for the Fort Detrick campus be increased to $16 million. The increase would allow NCI to complete priority facilities projects that will help, maintain FFRDC operations, and provide high-value support to the NCI mission, the research community, and to patients diagnosed with cancer.
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES [Provided, That not less than $273,325,000 is provided for the Institutional Development Awards program.]	NIH requests this specific language be removed because it is not necessary to set-aside a specific amount in appropriations language, as NIGMS justification identifies the level of resources planned to be devoted to this program in FY 2016.
NATIONAL LIBRARY OF MEDICINE Provided, That of the amounts available for improvement of information systems, $4,000,000 shall be available until September 30, [2016]*2017*:	NIH requests this language change to ensure continuation of two-year funding availability.
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES [Provided further, That at least $474,746,000 is provided to the Clinical and Translational Sciences Awards program]	NIH requests this specific language be removed because it is not necessary to set-aside a specific amount in appropriations language, as NCATS justification identifies the level of resources planned to be devoted to this program in FY 2016.
OFFICE OF THE DIRECTOR *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.*	NIH requests this specific language in order to provide clarity regarding the NIH Director's ability to use the one percent transfer authority, as provided in authorizing language.

Language Provision	Explanation/Justification
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, $128,863,000, to remain available [through September 30, 2019] *until expended*.	NIH requests that the word 'demolition' be added to the appropriations language. In addition, NIH requests that language reverts back to previous language in the Consolidated Appropriations Act, 2012 (P.L.112-74) … by adding back 'until expended' to provide NIH maximum flexibility to administer these resources.
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES [For an additional amount for National Institute of Allergy and Infectious Diseases to prevent, prepare for, and respond to Ebola domestically and internationally, including expenses related to carrying out section 301 and title IV of the PHS Act, $238,000,000, to remain available until September 30, 2016: Provided, That such amount is designated by the Congress as an emergency requirement pursuant to section 251(b)(2)(A)(i) of the Balanced Budget and Emergency Deficit Control Act of 1985.]	NIH requests that this specific language be removed because it was provided as one-time emergency funding for this program.

AUTHORIZING LEGISLATION

(Dollars in Thousands)	FY 2015 Amount Authorized	FY 2015 Appropriations Act	FY 2016 Amount Authorized	FY 2016 President's Budget
National Institutes of Health:				
Section 301 and Title IV of the PHS Act	$29,369,000	$29,369,000	$30,236,511	$30,236,511
Section 330B(b)(2) of the PHS Act[1]	$150,000	$150,000	$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] This represents a mandatory appropriation, for which FY 2015 was authorized and appropriated in the Protecting Access to Medicare Act of 2014 (P.L. 113-93), and for which reauthorization is proposed for FY 2016.

APPROPRIATIONS HISTORY

Fiscal Year	Budget Request to Congress	House Allowance	Senate Allowance	Appropriation [1]
FY 2007	$28,578,417,000	$28,479,417,000 [2]	$28,779,081,000 [2]	$29,030,004,000 [3]
FY 2008	$28,849,675,000	$29,899,004,000	$30,129,004,000	$29,312,311,000 [4]
FY 2008 Supp.				$150,000,000
FY 2009	$29,457,070,000	$30,607,598,000	$30,404,524,000 [5]	$30,545,098,000
FY 2009 ARRA				$10,400,000,000
FY 2010	$30,988,000,000	$31,488,000,000	$30,988,000,000	$30,934,413,000 [6]
FY 2011	$32,136,209,000		$31,989,000,000	$30,935,000,000 [7]
FY 2012	$31,979,000,000		$30,630,423,000	$30,852,187,000 [8]
FY 2013				
Base	$30,852,187,000		$30,810,387,000	$30,929,977,000 [9]
Sequestration				-1,552,593,211
Subtotal	$30,852,187,000		$30,810,387,000	$29,377,383,789
FY 2014	$31,323,187,000		$31,176,187,000	$30,142,653,000
FY 2015	$30,353,453,000		$30,084,304,000	$30,311,349,000 [10]
FY 2016	$31,311,349,000 [11]			

[1] Does not include comparability adjustments. Superfund and Type 1 Diabetes are included except where indicated.

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

[3] 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.

[4] 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.

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

[6] 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 percent transfer to HHS of $4,587,000.

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

[8] 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.

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

[10] Excludes Ebola-related funding. Includes Program Evaluation Financing of $715,000,000.

[11] Includes Program Evaluation Financing of $847,489,000.

NARRATIVE BY ACTIVITY TABLE

(Dollars in Millions)	FY 2014 Actual	FY 2015 Enacted[1]	FY 2016 President's Budget	FY 2016 Request +/- FY 2015 Enacted
Program Level[2]	$ 30,070	$ 30,311	$ 31,311	$ 1,000
FTE	18,048	18,150	18,150	0

[1] Excludes Ebola-related funding.

[2] Includes Mandatory Type 1 Diabetes and Superfund in FY 2014, FY 2015 and FY 2016; includes NLM Program Evaluation ($8.20 million) in FY 2014; also includes NIGMS Program Evaluation funding of $715 mllion in FY 2015 and $847.5 million in FY 2016.

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

Allocation Methods: Competitive Grants; Contract; Intramural; Other

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

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.[15] Older Americans are not just living longer; they are staying healthy and active longer. Rates of reported risk factors for chronic disease (e.g., uncontrolled low-density lipoprotein (LDL) or high blood pressure, smoking, etc.) have dropped by more than 10 percent since 1999. At age 65, Americans today can expect to live 19.2 more years, or 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.[16] The fastest growing demographic group in the United States consists of individuals living beyond the age of 85. We can attribute these remarkable improvements, in 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.[17] 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 and prevention strategies, as well as safe and effective surgical and catheter-based procedures to open clogged coronary arteries. Current NIH research focuses on elucidating new biological pathways, new treatment and prevention models, developing and understanding the value of new diagnostic and imaging tests, and enhancing device technologies for treatment.

Diabetes

In the recent past, adults diagnosed with diabetes during middle age lived 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 now 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.[18] These remarkable improvements are due largely to clinical trials supported by NIH. In addition, basic science research has unveiled genes that may be involved in the development and progression of diabetes. NIH research also is generating important

---

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

[16] 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.

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

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

insights into the prevention and management of diabetes, highlighting the importance of family support. Studies funded through the Diabetes Prevention Program also 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 the disease. For Type 1 Diabetes, progress toward the development of a fully reliable artificial pancreas provides hope for an end to the daily routine of finger sticks and insulin injections.

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 due to both treatment and prevention strategies based on NIH-funded research. 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 United States. However, tPA must be administered relatively soon after the onset of symptoms. Current estimates suggest that fewer than 10 percent of stroke patients are treated with the drug. Recent NIH-funded research has led to the revision of tPA administration guidelines to extend the timing from three hours to four and a half hours in some cases.[19,20] NIH researchers are currently working to improve public awareness of stroke and to educate high risk populations on the importance of seeking immediate medical attention in order to increase the number of those receiving this life-saving and disability-reducing treatment.

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. However, both incidence rates and mortality rates continue to decline for both men and women. NIH-funded research has contributed to the decrease in mortality, lowering the death rate per 100,000 people by 20 percent between 1990 and 2010. 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. Advances in genetic screening techniques have helped NIH-funded researchers identify genes that may influence the risk for lung cancer development and genetic errors that cause lung cancer.

HIV/AIDS

In the 30 years since HIV was first recognized, NIH has established the world's leading AIDS research program. Each year, 50,000 people in the United States become infected with HIV, the virus that causes AIDS. Currently, there are more than one million people in the United States and 35 million people globally who are living with HIV infection. In the early 1980s when the HIV/AIDS epidemic began, those infected with the virus were not likely to live longer than a

---

[19] Bankhead, C. Clot-busting drugs used more often in stroke. *MedPage Today*. August 23, 2013. http://www.medpagetoday.com/Cardiology/Strokes/41156

[20] Jauch, E.C., et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 44:870-947 (2013). http://stroke.ahajournals.org/content/44/3/870.full.pdf+html

few years. Now, thanks to research funded in large part by NIH, there are powerful treatments that can suppress the virus to undetectable levels, allowing those infected with it to live for many years. In fact, death rates have dropped by more than 13 percent, and a 20-year-old HIV-positive adult living in the United States or Canada who receives these treatments is expected to live into their early 70s, nearly as long as someone in the general population.[21] These treatments, combined with advances toward the development of an HIV vaccine and research to find a cure, mean the eradication of AIDS is possible with sustained effort.

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. Recent research studies also identified 55 genes linked to a tumor suppressor gene that can predict breast cancer survival, as well as a natural compound that can attack human epidermal growth factor receptor 2 (HER2) positive breast cancer cells. Scientists also conducted studies in mice in which they found a protein that reduces the risk that breast cancer will spread. In addition, a new imaging technique to improve diagnosis in women with dense breast tissue has been developed. 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

Prostate cancer is one of the most common cancers and the second leading cause of cancer-related death for men in the United States. 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. Current research focuses on increasing understanding of the epidemiology and genetics of prostate cancer and improving treatment and diagnostic options.

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. Nearly all cervical cancer is caused by human papillomavirus (HPV). 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. Ongoing efforts to scale up the use of the vaccines both in the United States and abroad are under way.

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 in reducing

[21] Samji H, Cescon A, Hogg RS, Modur SP, Althoff KN, Buchacz K, Burchell AN, Cohen M, Gebo KA, Gill MJ, Justice A, Kirk G, Klein MB, Korthuis PT, Martin J, Napravnik S, Rourke SB, Sterling TR, Silverberg MJ, Deeks S, Jacobson LP, Bosch RJ, Kitahata MM, Goedert JJ, Moore R, Gange SJ; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of IeDEA. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. PLoSOne. 2013 Dec 18;8(12):e81355.

preterm births, neonatal mortality, and other complications that increase the risk of infant death, 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 declined steadily since the 1970s, and continued to decline in 2013.

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 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 have begun to understand epigenetic changes that can occur in individuals and to identify genes that result in an increased risk of AMD. Scientists also are developing new technologies to improve imaging methods for diagnosis.

Hearing Loss

As a result of NIH efforts that led to statewide screening for hearing loss in newborns and infants, nearly all infants born in U.S. hospitals in 2010 were screened for hearing loss, up from as few as one-tenth of infants screened in 1993. NIH-supported research also 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 improved significantly 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 improved greatly 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. Between 1990 and 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.

Alzheimer's Disease

Alzheimer's disease is a progressive, irreversible brain disease that slowly destroys memory and thinking skills, and eventually even the ability to carry out the simplest tasks of daily living. Alzheimer's disease is currently the sixth leading cause of death in the United States and affects as many as five million Americans age 65 and older. As recently as 30 years ago, very little was known about Alzheimer's disease, but research supported by NIH and other organizations greatly expanded knowledge and understanding of brain function, risk factors, treatment, and prevention. One particular focus of research is in detecting the disease before symptoms appear, in the hope that treatment might be able to reverse the disease at this earlier stage. A recent study identified a set of 10 compounds in the blood that might be usable as risk factors for memory decline, opening up the possibility for doctors to measure dementia risk with a simple blood test. While much more remains to be discovered in each of these areas, recent research has led to more than 90 drugs in clinical trials for Alzheimer's disease with many more in the pipeline awaiting FDA approval to enter human testing.

Chronic Obstructive Pulmonary Disease (COPD)

COPD is a progressive disease that includes two main conditions that coexist: emphysema and chronic bronchitis. COPD is the third leading cause of death in the United States and a major cause of disability, which in many cases may be undiagnosed. The majority of COPD sufferers are current or former smokers over 40 years old. Large, multi-center, NIH-funded clinical trials are evaluating the efficacy of several treatments in order to reduce the disability and costs associated with COPD. In addition, new studies are examining the genetic contributions, susceptibility, and disease progression of COPD, as well as attempting to understand the mechanisms that link COPD to cardiovascular health.

Chronic Pain

Chronic pain is a debilitating symptom of many long-term diseases and a major cause of disability among Americans. The NIH Pain Consortium was established to enhance pain research and promote collaboration among researchers across NIH. NIH-funded research has led to many advances in understanding the mechanisms behind chronic pain, including genetic contributions and neurological pathways, as well as developing new ways to manage and treat chronic pain.

Science Advances from NIH Research

NIH-funded scientists report thousands of new findings every year across the spectrum of biomedical science, from basic research to clinical studies and beyond. Many of the basic science discoveries build over time until they can be pieced together and translated into diagnostics or treatments to improve health. A few of the many recent NIH research accomplishments are listed below.

Ebola Vaccine Research and Development

The on-going Ebola virus disease epidemic in West Africa reminds us that viruses remain a threat to human health and can emerge at any time with devastating consequences. The need for a fully protective vaccine to prevent Ebola transmission is a priority. While NIH has supported

the development of such a vaccine since 2001, the epidemic that arose in early 2014 refocused attention on this need and expedited the development process, resulting in potentially beneficial experimental vaccine candidates.

In September 2014, a Phase I clinical trial assessed the safety, efficacy, and immunogenicity of an intramuscular vaccine co-created by NIH and GlaxoSmithKline. The vaccine causes infected cells to express a specific Ebola protein that, in turn, prompts an immune response. Prior to human study, non-human primates inoculated with this vaccine developed both antibody and cellular (T-cell) responses sufficient to protect them from the Ebola virus. Results indicated this vaccine was well-tolerated and elicited anti-Ebola antibody responses in the healthy adult volunteers. Moving forward, NIH plans to conduct Phase II/III studies in Liberia to assess the efficacy and safety of this vaccine compared to other Ebola vaccine candidates prior to wider vaccine distribution.

Another promising vaccine candidate began Phase I trials in October 2014 in thirty-nine healthy volunteers. The vesicular stomatitis virus (VSV) Ebola vaccine studies are being conducted in collaboration with the U.S. Department of Defense and NewLink Genetics Corp. A parallel study is on-going at the Walter Reed Army Institute of Research to evaluate in real time the vaccine's safety when provided at different dosages and compare the immune responses induced by one injection to the response to two doses.

Atlas of the Developing Brain

NIH-supported scientists contributed to the first comprehensive 3-D atlas of gene expression in the developing human brain as part of a larger project to profile gene expression throughout the course of brain development. Scientists gathered the data using a variety of genomic and imaging techniques on intact human pre-natal brains. The results provide a powerful map to pin brain areas to genes tied to neurodevelopmental disorders and human-specific brain functions. This resource will help reveal the early roots of brain-based disorders, such as autism and schizophrenia.

Gut Microbes Linked to Autoinflammatory Disease

Rheumatoid arthritis is a chronic inflammatory disorder that causes pain, swelling, and stiffness in joints when the immune system mistakenly attacks the body's own tissue. The immune system is influenced by the microbiome, which consists of trillions of microbes – bacteria, fungi, and viruses – that live in and on the body. NIH-supported researchers found that 75 percent of people with new-onset, untreated rheumatoid arthritis had the bacterium *Prevotella copri* in their intestinal microbiome. To test whether *P. copri* could influence inflammation, the team administered the bacteria to healthy mice so that the bacteria became part of their gut microbiome. Mice were then given a chemical that induced colitis, a model of gut inflammation. Animals with *P. copri* developed more severe symptoms than the mice that had not received the bacteria. The finding provides further evidence for a potential role for bacteria in this autoimmune disease.

Another recent NIH-funded study revealed that diet-induced changes to intestinal bacteria can influence susceptibility to autoinflammatory disease. The results could help guide new, dietary approaches to treat autoinflammatory diseases in susceptible people.

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 (called Cas9) that is involved in a bacterium'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 valuable for numerous applications, including conducting large-scale genetic screens in mammalian cells (recently validated by NIH-funded scientists), as well as the promise of new treatments for genetic diseases. Furthermore, the recent discovery of the specific structure of the Cas9 protein opens up new possibilities to maximize the potential of the CRISPR technology to advance understanding of disease and accelerate development of treatments and cures.

Safe, Effective Gene Therapy for Hemophilia

Hemophilia is a rare bleeding disorder in which the blood fails to clot normally. Current treatments require a lifetime of frequent injections, often twice a week, of an expensive clotting factor called factor IX in order to restore normal clotting. A recent NIH-funded clinical trial used gene therapy to reprogram the body's own cells to produce factor IX using special viruses that have been engineered not to cause diseases. When adult men with hemophilia were given an intravenous dose of the therapy, patients with the higher dose improved markedly, with the effects lasting for the entire 4-year period of the study.

New Insights into Bariatric Surgery Outcomes

Researchers who followed adults and teens who have undergone bariatric surgery for severe obesity found that this type of treatment is both safe and effective. Adults who had undergone the procedure not only had substantial weight loss but also significant improvements in diabetes and cardiovascular disease risk factors after three years. Although weight loss did vary, and the maximum weight loss occurred during the first year, many individuals with diabetes before surgery experience partial remission, and significant improvements in blood pressure and lipid levels were seen in many patients.

A 3-D Scaffold Guides Stem Cells into Cartilage-Producing Cells

NIH-funded researchers developed a 3-D scaffold that guides the development of stem cells into specialized cartilage-producing cells, an approach that could allow for the creation of orthopedic implants to replace cartilage in patients with arthritis. The scientists applied human stem cells from adult bone marrow to a 3-D woven scaffold coated with viruses. The viruses were used to transfer the gene TGF-β3 gene into the cells. The TGF-β3 drives the cells to become chondrocytes, which are the type of cells found in cartilage. Cells within the artificial scaffold successfully differentiated into chondrocytes within two weeks and created a cartilage-like extracellular matrix within four weeks. This approach could allow for implants that restore function to a joint immediately and drive development of a mature, viable tissue replacement.

Nature-Inspired Surgical Glue Mends Hearts

Researchers developed a new biodegradable, biocompatible, and easily manipulated tissue adhesive that could allow for less invasive surgeries that do not require sutures or staples. Inspired by the footpad of insects and the thick, sticky secretions of slugs and sandcastle worms,

whose fluids can create bonds underwater, the research team set out to develop a similar gel-like material that could function as a stable, water-insoluble, and elastic surgical glue. The gel's base consisted of glycerol, a basic building block of lipids, as well as a naturally occurring fatty acid. When mixed with a special light-sensitive chemical, the resulting gel solidifies after being exposed to ultraviolet (UV) light for five seconds. The researchers found that the gel easily spread over a surface and adhered to tissues in wet conditions, and they tested the glue in several settings. The team demonstrated that the glue stayed attached to the beating hearts of rats and pigs without altering heart function. The glue also was able to seal a defect in the wall of a rat heart and to create a leak-proof seal in the carotid artery of pigs. The technology has been licensed to a company, and patents based on the study have been filed. Long-term experiments will be needed to further evaluate the gel before it can be tested in humans.

Blood Test for Solid Tumors

A simple blood test was shown to detect solid tumors rapidly and accurately, track their progression over time, and could possibly predict their response to treatment. Solid tumors include cancers of the brain, breast, colon, and other tissues and consist of abnormal masses of tissue that usually do not contain cysts or liquid areas. Cancers of the blood, like leukemia, usually do not form solid tumors. Lung cancer solid tumors are particularly difficult to detect. NIH-funded scientists used genetic data from the Cancer Genome Atlas (TCGA) database to develop a molecular signature for non-small-cell lung cancers. Using this signature and samples from patients with non-small-cell lung cancer, researchers designed a highly sensitive DNA-based blood test that accurately identified all patients with advanced lung cancer, as well as half of patients whose lung cancer was in its earliest stage. Efforts are now under way toward clinical trials to measure this technique and its potential to improve the detection of many different kinds of solid tumors. The technique also may be developed to monitor treatment progression and to predict disease outcome.

Isolating and Profiling the Cancer Cells that Cause Metastasis

One of the issues that makes treating cancer so difficult is that cells can shed from individual tumors and spread throughout the body in a process called metastasis. Often, these cells enter the bloodstream in low numbers and result in new cancerous growths that are resistant to treatment. A recent study invented a new method which, using microfluidic technology to manipulate tiny volumes of fluid, can isolate these circulating cancer cells from the bloodstream in patients with metastatic breast cancer. Isolating these cells from the blood will allow researchers to directly characterize the cells that cause metastasis, to discover both genetic changes that lead to metastasis and the treatments which might be more likely to target it successfully.

Structure of Hepatitis C Cell Surface Protein Important for Virus Entry

Hepatitis C is an infectious disease caused by a virus that attacks the liver, leading to inflammation. Most infections become chronic and, if left untreated, can cause severe liver disease or liver cancer. Some proteins on the surface of the hepatitis C virus (HCV) are constantly changing, which allows the virus to avoid the natural defenses of the body's immune system. Using X-ray crystallography, NIH-supported researchers have determined the structure of a protein on the surface of the HCV that allows it to bind to, and gain entry into, liver cells. This finding may help in developing a vaccine against HCV, as well as new inhibitors.

Using Tiny Sponges to Fight MRSA

Methicillin-resistant, Staphylococcus aureus bacteria, commonly known as MRSA, is a critical threat to public health. In the United States, MRSA causes more than 80,000 skin, lung, and blood infections and kills about 11,000 people each year. The bacteria cause their devastation by secreting a toxin that punches holes in the membranes of cells, causing their contents to leak and the cells to die. To prevent the toxin from weakening the cells, NIH-funded researchers developed a sponge that can trap and bind the MRSA toxin. These sponges were then injected into mice to evoke an immune system response that would protect the mice against future exposure to the MRSA toxin. This could be a new technique to fight bacterial infections without the use of antibiotics.

Toxin Kills HIV-Infected Cells

Researchers found that an HIV-specific poison can kill cells in mice in which the virus is still reproducing despite antiretroviral therapy. In an effort to identify a targeted poison that could complement antiretroviral therapy by killing HIV-infected cells, 3B3-PE38, a genetically designed, HIV-specific poison, was developed. This immunotoxin targets HIV-infected cells and, when taken inside cells, shuts down protein synthesis and triggers cell death. To test the poison, researchers infected 40 mice bioengineered to have a human immune system with HIV. After several months, the mice were given a combination of antiretroviral drugs for four weeks. Half the animals subsequently received a two-week dose of the immunotoxin in addition to the antiretrovirals, while the other half continued receiving antiretrovirals alone. The addition of the immunotoxin significantly reduced the number of cells with detectable virus in multiple organs. It also lowered the level of HIV in the blood. Additional research is needed before this can be tested in clinical trials.

Antibiotics to Treat Drug-Resistant Forms of Tuberculosis (TB)

Researchers designed and tested a class of new antibiotics to treat TB, a contagious disease caused by infection with *Mycobacterium tuberculosis* (Mtb) bacteria. TB is treated with antibiotic drugs, but the bacteria have evolved to become resistant to these medications. An NIH-funded research team set out to develop new drugs that could work against drug-resistant strains of Mtb but have minimal side effects. Researchers analyzed the structure of an existing antibiotic and made various chemical modifications to create a new class of agents that were active against both multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria. These compounds were not toxic in laboratory assays or in animals, and a subset of the compounds was highly effective against TB infections in mice. This work represents an initial step in the development of a new class of drugs to treat TB.

Technique Directs Immune Cells to Target Leukemia

In targeted immunotherapy, which directs the patient's own immune system to attack cancer cells, 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. Using a form of targeted immunotherapy, NIH-funded clinician-scientists induced remission in adults with an aggressive form of leukemia who had relapsed – a situation with typically poor prognosis. Of 16 patients who received the therapy, 14 were in complete remission within weeks of the T-cell infusion. Additional studies by NIH researchers found that targeted immunotherapy can treat not only cancers of the blood, but also other hard-

to-treat cancers, such as cancers of the epithelial cells that line the surface of the body, which comprise more than 80 percent of all cancers.

Drug Delivery System from Grapefruit Juice

Microscopic pouches made of synthetic lipids can serve as a carrier to protect drug molecules within the body and deliver them to specific cells. However, these synthetic carriers can pose obstacles, including potential toxicity, environmental hazards, and the cost of large-scale production. A naturally derived tiny particle found in grapefruit juice can be used to make micro-capsules that can safely deliver drugs and biologic agents to humans. Researchers involved in this study were searching for sources of edible, non-toxic, and plant-derived sources for drug delivery. Using these sources instead of mammalian or artificial sources could pose fewer potential health risks and be produced at a much lower cost. The grapefruit-derived molecules proved to be a safe, effective way to deliver some chemotherapy drugs in mouse models with no signs of adverse effects or toxicity. A phase I clinical trial is under way to determine whether the grapefruit-derived molecules can deliver anti-inflammatory drugs or chemotherapy drugs to targeted cells.

Mining a Treasure Trove of Big Data

Biomedical researchers and clinicians are generating mountains of digital data through DNA sequencing, biomedical imaging, and electronic health records. The next era of biomedical research will leverage the power of Big Data to advance scientific discovery. For instance, one researcher used a database that catalogued the DNA variation in patients to find new links among genes, diseases, and detectable physical or behavioral characteristics, such as cholesterol levels or body weight. Once the genes were linked to diseases, researchers mined the data to find associations between the diseases and physical or behavioral traits. One surprising finding they made was a link between elevated prostate specific antigen (PSA) and lung cancer. Other studies are now doing targeted searches of the 1percent of the human genome that codes for proteins, allowing for the rapid detection of new disease-causing mutations in patients with suspected genetic diseases. Two 2014 studies found that as many as 25 percent of undiagnosed patients were able to get a diagnosis using these new techniques. In the future, these links may be used to predict whether an individual will develop a particular disease or to identify a common biological mechanism underlying many diseases.

In addition to the treasure trove of DNA data, NIH-funded researchers are assembling a massive amount of data on the proteins in the human body to look at how and where genes are expressed. A team of researchers funded by several NIH Institutes and Centers examined tissue from multiple ages, tissues, and cell types and sequenced the amino acids that make up the proteins in each tissue, resulting in a map of the human proteome. The results included known products of 17,000 human genes - 84 percent of the known protein-coding genes in the genome - and 193 novel proteins that previously had not been identified, as well as a few genes which were expressed in unexpected places or times. This study and others like it offer a new trove of data to help other scientists understand human health and disease.

Telemedicine Catches Blinding Disease in Premature Babies

Retinopathy of prematurity (ROP) appears in more than half of all infants born at 30 weeks pregnancy or younger, although only about 5 to 8 percent of cases are severe enough to require treatment. In ROP, blood vessels in the retina begin to grow abnormally, which can lead to

scarring and detachment of the retina. Early diagnosis and prompt treatment is the best prevention for vision loss from ROP; thus, routine screening by an ophthalmologist is recommended for all babies who are born at gestational age 30 weeks or younger or who weigh less than 3.3 pounds at birth. NIH-supported researchers recently piloted a telemedicine strategy that sent photos of babies' eyes to a distant image reading center for evaluation by non-physicians trained to recognize signs of severe ROP. In the study, the non-physician readers accurately identified 90 percent of infants that ophthalmologists referred for further evaluation and potential treatment. The approach, if adopted broadly, could help ease the strain on hospitals with limited access to ophthalmologists and lead to better care for infants in underserved areas of the country.

Expanding the Genetic Alphabet

DNA is comprised of four chemical bases that form two base pairs (adenine with thymine and cytosine with guanine). The order of these pairs defines genes and other essential information for cell function. Synthetic biology aims to redesign natural biological systems for new purposes, and scientists previously expanded the genetic alphabet to include several unnatural base pairs in DNA. New experiments conducted by NIH-supported researchers have created the first living organism that can grow and reproduce using DNA base pairs that are not found in nature. This step of incorporating unnatural base pairs into an organism marks a substantial leap in the field and eventually could aid development of novel protein therapeutics, diagnostics, and lab reagents to have specific functions.

Placental Microbiome

The placenta is a vital organ that develops during pregnancy to deliver food and oxygen to the growing fetus via the umbilical cord. Until recently, the placenta was thought to be germ-free and sterile to keep the baby safe from infection. However, that left scientists at a loss to explain the complex array of microbes in babies' guts just a week after birth. Recently, a research team led by a recipient of an NIH Director's New Innovator Award discovered that the placenta itself has its own microbes. They also found that the placental microbes from babies born earlier than 37 weeks (preterm births) had a significantly different collection of microbes compared to those of babies carried to full term. This observation could have clinical significance if further research indicates that specific microbes or predictable shifts in the bacterial community explain why some infants are more likely to be born preterm. If this is the case, then early diagnostic testing may help identify women at risk for preterm birth and possibly lead to ways to encourage full-term pregnancies.

Advances in the Treatment of Sickle Cell Disease

Sickle cell disease is a genetic blood disorder that causes defective hemoglobin, the protein in red blood cells that carries oxygen. It affects millions worldwide, including approximately 100,000 people in the United States. The disease disproportionately affects African Americans, and current treatments are largely ineffective. NIH-funded studies are addressing this need from multiple angles, and several therapies hold promise. A recent study showed that a stem cell transplant from a healthy relative could reverse the disease in 87 percent of patients. NIH research also is working towards a drug therapy for sickle cell disease. Through a collaborative agreement, researchers at the National Center for Advancing Translational Sciences' (NCATS) Therapeutics for Rare and Neglected Diseases (TRND) program and AesRx, a biopharmaceutical company, developed a drug candidate to treat sickle cell disease that

specifically targets the underlying disease mechanism. TRND and AesRx researchers worked together to develop Aes-103 through a Phase II clinical trial to evaluate safety and effectiveness. The success of this trial resulted in the recent acquisition of the drug by a pharmaceutical company that will advance the clinical development activities required for regulatory approval and commercialization.

FUNDING HISTORY

Fiscal Year	Amount[1]
2012[2]	$30,852,187,000
2013[3]	
Base	$30,695,855,975
Sequestration	-$1,552,593,211
Total Post-Sequestration	$29,143,262,764
2014 Actual [2]	$30,061,862,000
2015 Enacted [4]	$30,311,349,000
2016 Budget Request	$31,311,349,000

[1] Appropriated amounts include 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. Includes mandatory budget authority derived from the Special Type 1 Diabetes account; also includes NLM Program Evaluation ($8.20 million) in FY 2014, and NIGMS Program Evaluation financing of $715 mllion in FY 2015 and $847.5 million in FY 2016.

[2] FYs 2012 and 2014 appropriation includes the effect of Secretary's Transfers.

[3] FY 2013 appropriation includes the effect of sequestration, 0.2 percent across-the-board rescission, and Secretary's Transfers.

[4] Excludes Ebola-related funding.

SUMMARY OF THE REQUEST NARRATIVE

The FY 2016 President's Budget request would provide $31.3 billion to NIH, which is $1.0 billion above the FY 2015 Enacted level.

The following summary references program level funding, which includes discretionary budget authority in the Department of Labor, Health and Human Services, and Education, and Related Agencies appropriation and in the Department of the Interior, Environment, and Related Agencies appropriation (dedicated to the Superfund Research program), mandatory budget authority derived from the Special Type 1 Diabetes account, and National Institute of General Medical Sciences funding under Section 241 of the Public Health Service Act.

Research Project Grants (RPGs)

The FY 2016 President's Budget would provide $17.2 billion for RPGs, which is $873 million more than the FY 2015 Enacted level estimate. This amount would fund 10,303 Competing RPGs, or 1,227 more than estimated for the FY 2015 Enacted level. It also supports 23,303 Noncompeting RPGs, 130 less than the FY 2015 Enacted level. In addition, the Competing RPGs average cost of approximately $461,000 would be very similar to the FY 2015 Enacted level.

- **Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR)** The FY 2016 President's Budget would provide $765 million for SBIR/STTR program grants, which is $49 million above the FY 2015 Enacted level. The minimum set-aside requirement increased from 3.30 percent in FY 2015 to 3.45 percent for FY 2016.

Research Centers

The FY 2016 President's Budget would provide $2.6 billion for Research Centers, which is $63 million less than the FY 2015 Enacted level. It would fund 1,399 grants, 42 more than the FY 2015 Enacted level.

Other Research

The FY 2016 President's Budget would provide $1.9 billion for this mechanism, which is $38 million more than the FY 2015 Enacted level. It would fund 6,527 grants, which is 337 more than the FY 2015 Enacted level.

Training

The FY 2016 President's Budget would provide $785 million for training which is $23 million more than the FY 2015 Enacted level. A two percent increase to stipend rates is proposed to maintain the stipend's purchasing power and offset the effects of anticipated inflation. It would fund 15,735 Full-Time Trainee Positions (FTTPs), which is 204 more than the FY 2015 Enacted level.

Research & Development (R&D) Contracts

The FY 2016 President's Budget would provide $2.9 billion for R&D contracts, which is $3.0 million less than the FY 2015 Enacted level. It would fund an estimated 2,095 contracts, which are 17 more than the FY 2015 Enacted level.

- **Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR)** The FY 2016 President's Budget includes a $79 million set-aside within the R&D Contracts mechanism for support of qualified SBIR/STTR contracts. The minimum set-aside requirement increased from 3.30 percent in FY 2015 to 3.45 percent for FY 2016.

Intramural Research (IR)

The FY 2016 President's Budget would provide $3.52 billion for IR, which is $95 million more than the FY 2015 Enacted level. It accommodates mandatory pay cost increases for Federal civilian employees and military personnel, including the proposed 2016 pay raise of 1.3 percent, health insurance premium adjustments, and higher agency contributions to the Federal Employee Retirement System (FERS).

Research Management and Support (RMS)

The FY 2016 President's Budget would provide $1.58 billion for RMS, which is $19.5 million above the FY 2015 Enacted level. The amount covers mandatory pay cost increases for Federal civilian employees and military personnel attributable to the same factors described for the IR mechanism, such as the proposed 2016 pay raise of 1.3 percent, growth in health insurance premiums and higher FERS contribution rates.

Office of the Director (OD)

The FY 2016 President's Budget would provide $1.44 billion for OD, which is $29 million more than the FY 2015 Enacted level.

- **Other than Common Fund**

  The $877 million allocated for OD elements other than the Common Fund is $9.0 million above the FY 2015 Enacted level. This segment includes $158 million for Strategic Pediatric Research, $13 million more than the FY 2015 Enacted level.

- **Common Fund (CF)**

  Approximately $566 million is allocated for CF-supported programs. This amount is $20 million above the FY 2015 Enacted level and represents at least 1.9 percent of NIH total FY 2016 discretionary budget authority. It also includes $12.6 million from the Pediatric Research Initiative Fund, the same as the FY 2015 Enacted level.

Building & Facilities (B&F)

The FY 2016 President's Budget provides $145 million for infrastructure sustainment projects associated with the B&F program, which is $8 million above the FY 2015 Enacted level. This amount includes $16 million for facility repair and improvement activities at the National Cancer Institute's Frederick, Maryland, facility.

Superfund Research Program

The FY 2016 President's Budget would provide $77 million which is the same amount as the FY 2015 Enacted level.

Type 1 Diabetes

The FY 2016 President's Budget would provide $150 million in mandatory funding for Type 1 Diabetes research grants, which is the same as the FY 2015 Enacted level.

Program Evaluation Financing

The FY 2016 President's Budget would provide $848 million for Program Evaluation Financing purposes, which is $132 million above the FY 2015 Enacted level.

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.

Clearly linking public health improvements to NIH-funded research remains a challenge. By its nature, research is a long-term and accumulative 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, 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 instance, 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. One example of portfolio analysis conducted in support of a new Common Fund program area is the 4D Nucleome program, launched in FY 2015. Analysis of the NIH's investment in related scientific areas revealed limited large-scale efforts in genome-wide analysis and computational analyses. The 4D Nucleome program initiatives are designed to fill these gaps, providing a strategic investment that aims to catalyze this emerging scientific area.

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 (RePORTER) at http://projectreporter.nih.gov. In 2014, the NIH led the way in extending its reporting capabilities to other agencies by creating Federal RePORTER (http://federalreporer.nih.gov), a single searchable database of research projects funded by science agencies across the Federal government. In 2015, the NIH will release proof-of-concept software that will allow the Agency's program administrators to simultaneously search multiple databases for long-term research outcomes relevant to their programs. Efforts are also underway to increase the data integration and informatics capabilities needed to support portfolio analysis 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 outputs 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. The NIH is currently exploring strategies to implement the SMRB recommendations to employ a more comprehensive, systematic, and strategic approach for building the evidence base for biomedical research.

OUTPUTS AND OUTCOMES

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-1.1 By 2016, explore biological or bio-behavioral pathways through which physical activity and weight control may affect cancer prognosis and survival. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Develop trans-disciplinary teams on 3 research projects that bring together behavioral intervention expertise, cancer biology, and other basic and clinical science disciplines relevant to the pathways of interest. (In Progress)	Identify potential pathways through which physical activity interventions, weight control interventions, or a combination of these interventions affect cancer prognosis among cancer survivors, or conduct intervention studies to test these effects on relevant biomarkers.	Evaluate promising strategies for obesity prevention and treatment in real-world settings, and harness technology and tools to advance obesity research, and to improve health and survival among cancer patients.	N/A
SRO-1.2 By 2016, compare the effectiveness of two treatments for over active bladder syndrome among women. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Recruitment of over 300 women for the study. (In Progress)	Evaluate any changes in urine biomarker levels in approximately 250 women that may be associated with one of the two treatments.	Analysis completed for Overactive Bladder Questionnaire Short form and Treatment Satisfaction Survey.	N/A
SRO-1.3 By 2017, complete testing of the hypothesized mechanism of treatment effect of three novel treatment approaches for mental disorders, and advance one promising intervention into further clinical trial testing (e.g., pilot studies or efficacy trials). (Output)	FY 2015: Result Expected Dec 31, 2015 Target: (FY15) Identify one hypothesized mechanism of treatment effect for novel interventions that is based on emerging neuroscience or basic behavioral science of mental disorders.	(FY15) Identify one hypothesized mechanism of treatment effect for novel interventions that is based on emerging neuroscience or basic behavioral science of mental disorders.	(FY16) Initiate testing of hypothesized mechanism of treatment effect of one novel intervention, and determine whether the intervention should progress further to clinical testing.	N/A
SRO-1.4 By FY 2016, advance a novel drug candidate for a disease that affects the nervous system to the point of preparedness for human studies. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Complete medicinal chemistry optimization for one project (compound) in the Blueprint Neurotherapeutics Network. (In Progress)	Initiate toxicology studies enabling an Investigational New Drug (IND) application for a Blueprint Neurotherapeutics Network project.	File an Investigational New Drug application with the FDA for a Blueprint Neurotherapeutics Network project.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 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 2014: Result Expected Dec 31, 2014 Target: 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	N/A
SRO-2.2 By 2019, assess the efficacy of one to two anti-inflammatory therapy for cardiovascular disease (CVD) in HIV-infected individuals. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Develop trial protocol and begin patient enrollment. (In Progress)	Achieve cumulative enrollment of 140 patients and conduct follow-up visits.	Complete enrollment of 200 subjects and conduct follow-up visits.	N/A
SRO-2.3 By 2018, evaluate the impact of two community-level combination prevention packages (which include universal HIV testing and intensified provision of HIV antiretroviral therapy and care) on population-level HIV incidence in the developing world. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Initiate a trial of a combination prevention approach to preventing HIV infections on a population level in Zambia and South Africa (In Progress)	Complete target enrollment of 52,500 in the population cohort	Complete annual follow-up visits and HIV incidence evaluations	N/A
SRO-2.4 By 2020, increase the number of potential treatment options for communication disorders that are being tested in clinical trials by adding one new treatment option per year. (Outcome)	FY 2015: Result Expected Dec 31, 2015 Target: Initiate testing one new potential treatment option for a balance disorder.	Initiate testing one new potential treatment option for a balance disorder.	Initiate testing one new potential treatment option for a TBD communication disorder.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-2.6 By 2020, investigate the pathways and mechanisms of how seven environmental agents can alter epigenetic processes such as DNA methylation, recruitment of specific histone modifications, and chromatin remodeling to better determine if these changes can be inherited. (Output)	FY 2015: Result Expected Dec 31, 2015 Target: Generate epigenomic maps of three cell types, exposed to four environmental chemicals.	Generate epigenomic maps of three cell types, exposed to four environmental chemicals.	Assess transgenerational effects of 6 exposures in 3 generations of animals.	N/A
SRO-2.9 By 2015, advance understanding of social determinants of health and health disparities using multilevel, transdisciplinary 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 transdisciplinary 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)	Implement intervention models for reducing health disparities/inequities in various populations and identify commonalities for interventions in various underserved populations.	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)	Finalize 8 datasets (including ultrasound, anthropometry and physical exam data) and begin analyses of these datasets.	Continue analyses of IFED datasets and prepare a draft manuscript regarding the estrogenic effects of soy formula on infant development.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 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 a suite of studies to support efficacy evaluation and licensure of an HIV vaccine.	N/A	N/A
SRO-3.8 By 2018, 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% (Target Not Met). 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 85% of cases.	Complete hormone receptor scoring for 100% of cases.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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 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. Previous Target Identify at least one molecular pathway suitable for targeting in the patient cohort. (Target Met)	Complete a clinical pilot study in a cohort of pediatric patients with a disorder of the immune system	Identify at least one molecular pathway based on genetic analysis suitable for therapeutic targeting in a pediatric cohort of patients with an immune-mediated disease.	N/A
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 Phase 2 clinical testing of a novel compound	Complete phase 2 clinical studies of a candidate compound.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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)	Advance three projects to integration of individual organ or system chips into a multiple tissue chip or organ microsystem.	Completion of program towards integrated organ systems.	N/A
SRO-4.1 By 2016, enable 1-3 Bridging Interventional Development Gaps (BrIDGs) projects to have sufficient pre-clinical data for therapeutic agents in order to apply for Investigational New Drug (IND) approval from the FDA. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Select 1-3 projects for which the BrIDGs program will generate pre-clinical data. (In Progress)	Complete contracts for and initiate 1-3 projects that were selected.	Generate data to enable IND application on the 1-3 compounds for the projects that were selected.	N/A
SRO-4.2 By 2017, develop, adapt, and test the effectiveness of health promotion and disease prevention interventions in Native American (NA) populations that are culturally appropriate and promote the adoption of healthy lifestyles. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Build partnerships with three NA communities to incorporate a community-based participatory research approach to adapt, develop, and test interventions. (In Progress)	Identify, develop , and adapt three multilevel interventions for testing in Native American communities	Test three interventions in NA communities using rigorous study designs to test the effectiveness or efficacy of interventions.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-4.4 By 2016, discover the molecular basis for 30 rare diseases. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Enroll patients with rare or undiagnosed diseases into studies (In Progress)	Discover the molecular bases of 15 rare diseases	Discover the molecular bases of an additional 15 rare diseases	N/A
SRO-4.5 By 2016, test a targeted nanoparticle for imaging and drug delivery to atherosclerotic plaque in animal models. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Demonstrate targeted delivery of statin-loaded HDL nanoparticles to atherosclerotic plaque in rabbits and assess inflammation using 18F FDG. (In Progress)	Correlate rabbit inflammation imaging studies with histochemistry to confirm efficacy of nanoparticle treatment.	Extend the studies into a pre-clinical pig model to assess targeted delivery and efficacy in reducing inflammation.	N/A
SRO-4.6 By 2016 use animal models to identify 3 new targets and/or molecular mechanisms that could be used in the development of interventions that enhance male fertility. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Identify one new molecular pathway governing the generation of sperm and/or sperm function. (In Progress)	Identify one new pathway/mechanism that regulates spermatogenic stem cells in their decision making process governing cell renewal vs. cell differentiation.	Identify one epigenetic mechanism regulating spermatogenesis.	N/A
SRO-4.7 By 2016, determine the safety and effectiveness of two first-in-class treatments for nonalcoholic fatty liver disease in adults and children. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Enroll target number of pediatric patients with NAFLD for cysteamine treatment trial. (In Progress)	Finish data collection in obeticholic acid treatment trial of adult patients with NASH.	Analyze data from pediatric and adult NAFLD treatment trials.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-5.2 By 2018, (a) identify genetic factors that enhance or reduce the risk of development and progression of chronic obstructive pulmonary disease (COPD) and (b) validate new genetic and clinical criteria that may be added to COPD classification and contribute to better and/or earlier diagnosis or prognosis of the disease. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Complete Genome-wide Association analysis of the original 10,000 subjects to discover 3 statistically significant genetic risk factors for COPD. (In Progress)	Using analysis of genetic and clinical data from the original 10,000 subjects, identify 1-3 COPD sub-classes that can then be tested for prognostic potential.	Analyze longitudinal for the first 1000 five year follow-up visits to identify 1-3 predictors of lung function decline.	N/A
SRO-5.3 By 2020, identify risk and protective alleles that lead to one novel therapeutic approach, drug target, or pathway to prevention for late-onset Alzheimer's disease. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Complete Discovery Phase whole genome sequencing and analysis of 582 family members from 111 families with late onset AD to identify genomic regions associated with increased risk of AD; sequencing of the coding regions of the DNA (whole exome sequencing) of 5,000 cases / 5,000 controls for both risk raising and protective loci; and whole exome sequencing and analysis of one individual from ~1,000 additional AD families to identify regions associated with increased risk for protection from AD (In Progress)	Initiate Replication Phase to validate genes / regions of interest identified from case-control and family sequencing in ~50,000 samples from well phenotyped individuals by targeted sequencing and/or genotyping.	Initiate analysis and confirmation of genes identified in the Discovery Phase	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-5.4 By 2017, address the growing public health problem of antimicrobial resistance by discovering four to six new therapeutic candidates and assessing two novel approaches/ regimens designed to preserve existing antimicrobials. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Discover two new candidate therapeutics for infections where resistance poses a significant public health threat. (In Progress)	Evaluate optimized treatment strategies to reduce the risk of antimicrobial resistance.	Discover two additional new candidate therapeutics for infections where resistance poses a significant public health threat.	N/A
SRO-5.5 By 2018, complete pre-commercial development of a point-of-care technology targeted for use in primary care setting. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Identify 6 enabling technologies with potential clinical use in primary care setting. (In Progress)	Establish feasibility of use of 3 to 4 identified technologies through preliminary testing.	Complete pilot clinical studies on 1 to 2 prototype devices.	N/A
SRO-5.6 By 2017, develop, evaluate, refine, and/or promote strategies for preventing prescription drug abuse and its consequences. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Develop and disseminate medical education curricula on pain and substance abuse (In Progress)	Develop, test or disseminate strategies to prevent prescription drug abuse, including the development of pain medications with reduced abuse potential	Develop, test or disseminate strategies to enhance the use of naloxone for overdose prevention	N/A
SRO-5.7 By 2016, the members of the National Dental Practice-based Research Network will contribute to the scientific basis for common dental procedures and improve the quality of dental care in community practices by conducting research studies in dental practices. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: By 2014, expand the number of participating dental practitioners from 1500 to 3000. (In Progress)	By 2015, design 10 studies nominated by practitioners as relevant to their practices.	By 2016, contribute to clinical decision-making based on evidence gained by the NPBRN studies.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-5.9 By 2017, determine the potential contributions of infectious agents to the underlying etiology of urologic chronic pelvic pain syndromes (UCPPS). (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Obtain 300 biological samples and corresponding clinical data from UCPPS patients and control subjects suitable for the study of infectious agents, including potential contributions to disease etiology and symptom variation (e.g., flare). (In Progress)	Assess 150 biological samples through complementary methods to characterize urologic microbial profiles of UCPPS patients and control subjects and through linking to associated clinical data relate profiles to patient characteristics, including symptoms and risk factors.	Complete analyses of differences in the urologic microbiome of UCPPS patients/controls by sex and according to stratification based on symptom profiles, correlations of flare events, and profiles of inflammatory markers.	N/A
SRO-5.10 By 2020, assess the effectiveness of five to seven interventions that focus on eliminating health disparities by utilizing community partnerships to conduct intervention research that will foster sustainable efforts at the community level that will impact disparate conditions. (Output)	FY 2015: Result Expected Dec 31, 2015 Target: Initiate the implementation of the Phase I plan and pilot, including baseline data.	Initiate the implementation of the Phase I plan and pilot, including baseline data.	Identify adaptive strategies and collect first year assessment variables	N/A
SRO-5.11 By 2018, develop and test three to five strategies for symptom management that reduce the effects of acute and chronic illness. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Initiate testing of one biological/genomic mechanism associated with symptoms or symptom clusters that has the potential to play a role in managing or assessing symptoms. (In Progress)	Develop one novel strategy for managing symptom clusters and that improves health outcomes such as HRQoL.	Test one novel strategy for managing symptom clusters and that improves health outcomes such as HRQoL.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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)	A formal process of prioritizing compounds for more extensive toxicological testing will be evaluated and used	N/A	N/A
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)	FY 2014: N/A Target: Develop materials to help academic officials address underage and harmful drinking and other substance use by their students. (In Progress)	Evaluate the effectiveness of screening and brief intervention for alcohol and other drug use in a variety of settings.	Develop interventions to prevent underage substance use, abuse and addiction in special populations.	N/A
SRO-6.1 By 2023, perform comparative effectiveness studies to test five therapies for prevention or treatment of type 2 diabetes. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Launch enrollment for two Restore Insulin Secretion protocols (In Progress)	Analyze data on complications in the Diabetes Prevention Program Outcomes Study	Enroll at least 2200 participants in Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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)	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	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, acceptability and efficacy of oral pre-exposure prophylaxis (PrEP) and topical microbicides for prevention of sexual transmission of HIV in women. (Target Met)	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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)	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	N/A
SRO-7.1 By 2016, assess the efficacy of a novel microbicide delivery system for the prevention of HIV. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Continue enrollment and follow up of a phase III trial of a novel microbicide delivery system. (In Progress)	Complete follow up of a phase III trial of a novel microbicide delivery system	Complete data analysis on the safety and/or efficacy of a novel microbicide delivery system	N/A
SRO-7.2 By 2018, develop an evidence-based, online resource to help people who have low back pain and their health care providers apply clinical evidence to individual circumstances when weighing treatment options. (Output)	FY 2015: Result Expected Dec 31, 2015 Target: Collect data on pain and function from Spine Patient Outcomes Research Trial participants 8 years after joining the study.	Collect data on pain and function from Spine Patient Outcomes Research Trial participants 8 years after joining the study.	Develop individualized models of patient outcomes following surgical or non-operative treatment for common causes of surgery for low back pain (e.g., intervertebral disc herniation, lumbar spinal stenosis, and degenerative spondylolisthesis)	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-7.3 By 2016, develop and/or evaluate one to four interventions using mobile technology to improve treatment delivery and adherence for addiction and related health consequences. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Develop and/or test 2-4 substance abuse treatment or medication adherence interventions using mobile technology (In Progress)	Continue to develop and/or test substance abuse treatment or medication adherence interventions using mobile technology	Identify next steps for testing or deployment of 2-4 substance abuse treatment or medication adherence interventions using mobile technology	N/A
SRO-8.2 By 2017, identify circuits within the brain that mediate reward for (1) drugs, (2) non-drug rewards such as food or palatable substances, and (3) aversion to drug effects, and (4) determine the degree of overlap between these circuits. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Identify drug-activated reward circuits (In Progress)	Identify non-drug activated reward circuits and compare with drug-activated reward circuits	Support research to compare and contrast rewarding versus aversive pathways in response to substances of abuse	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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. (Outcome)	FY 2013: NIH researchers identified three influences on sustainability of research-tested interventions in service systems such as 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)	Identify three (3) key factors influencing the scaling up of research-tested interventions across large networks of services systems such as primary care, specialty care and community practice. (Outcome)	Initiate testing of hypothesized mechanism of treatment effect of one novel intervention, and determine whether the intervention should progress further to clinical testing.	N/A
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)	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
SRO-9.2 By 2018, identify culturally appropriate, effective stroke prevention/intervention programs in minority communities. (Outcome and Efficiency)	FY 2013: Completed testing of a culturally tailored intervention in an underserved minority community and demonstrated an increased 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)	Initiate enrollment in two studies testing culturally tailored interventions to reduce health disparities in stroke.	Complete patient follow-up in a study testing a clinical program for improved blood pressure control in racial/ethnic minority populations.	N/A
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)	N/A	N/A	N/A
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. Previous target: Continue recruitment to 1134 subjects. (Target Met)	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	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
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]) 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)	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 [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]	(Integration [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] (Deployment [Dep]) Conduct priority deployment activities to enable user accessibility and skill development within 2 years from the onset of integration.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
CBRR-3 By 2016, develop diagnostic definitions and outcome measures for use in clinical research studies on chronic lower back pain (cLBP). (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Develop framework for standardized diagnostic definitions for use in clinical research studies on cLBP. (In Progress)	Disseminate information about development and validation of standardized research diagnostic measures for cLBP. (For example, report to NIH Pain Consortium and publication in peer reviewed journal.)	Test standardized research diagnostic measures for cLBP.	N/A
CBRR-5 By 2015, implement and evaluate leadership forums in cancer control planning in select low and middle income countries. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Develop the content of 2 leadership forums that will serve as a basis for developing and implementing national cancer control plans. (In Progress)	Organize, implement, and evaluate leadership forums in two regions of the world.	N/A	N/A
CBRR-7 By 2017 expand the scope and reach of the National Ophthalmic Diseases Genotyping and Phenotyping Network (eyeGENEÂ®), a national genetics research resource for rare inherited ocular diseases, by adding new patient records to the database, augmenting and refining the phenotypic data collected, and by increasing the number of registered researchers to 900. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Increase database and diagnostic genotyping to a total of 5,000 patient records. (In Progress)	Collect comprehensive phenotyping data from 500 patients, by using precision diagnostic, imaging tools and electrophysiological methods.	Create international collaborations for Network, extending into 3 foreign countries.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
CBRR-8 By 2017, characterize the three-dimensional atomic structure of 400 proteins of biomedical interest related to infectious agents. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Characterize the three-dimensional structure of 100 protein targets or other molecules of biomedical interest with regard to bacterial, viral, and eukaryotic pathogens (In Progress)	Characterize the three-dimensional structure of an additional 100 protein targets or other molecules of biomedical interest with regard to bacterial, viral, and eukaryotic pathogens	Characterize the three-dimensional structure of an additional 100 protein targets or other molecules of biomedical interest with regard to bacterial, viral, and eukaryotic pathogens	N/A
CBRR-10 By 2015, 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)	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	N/A
CBRR-11 By 2016, collect and make available for distribution 1200 well-characterized, high-quality human cell lines for use in genetic and genomic research. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Accept and make available to scientific researchers 400 new human cell lines. (In Progress)	Accept and make available to scientific researchers an additional 400 new human cell lines.	Accept and make available to scientific researchers an additional 400 new human cell lines.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
CBRR-12 Produce x-ray diffraction data for new protein structures that will enhance an existing x-ray resource for understanding basic biological processes. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Provide x-ray crystallographic data for 150 new structures of macromolecules of biomedical relevance to researchers worldwide (In Progress)	Provide x-ray crystallographic data for 160 new structures of macromolecules of biomedical relevance to researchers worldwide	Provide x-ray crystallographic data for 180 new structures of macromolecules of biomedical relevance to researchers worldwide	N/A
CBRR-13 By 2017, archive and annotate new protein structures to support research in human health and disease and drug development. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Annotate and archive 8,500 new protein structures (In Progress)	Annotate and archive 9,000 new protein structures	Annotate and archive 9,500 new protein structures	N/A
CBRR-14 By 2018, establish and utilize a national clinical network to conduct five stroke clinical trials using shared infrastructure and efficient processes. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Finalize master trial agreement with 100% of the Regional Coordinating Centers and the National Clinical Coordinating Center. (In Progress)	Use the network's Regional Coordinating Centers for patient recruitment in a stroke trial.	Initiate the first new trial to be conducted in the Stroke Network.	N/A
CBRR-15 By 2016, establish a resource database and tissue bank of 30 reference tissues (e.g., liver, skin, heart, bone) in which the relationship between genetic variation and gene expression is quantified and 3 additional molecular analyses are performed. (Output)	FY 2015: Result Expected Dec 31, 2015 Target: Demonstrate that at least 75% of a consensus list of replicated eQTLs are significant in at least 1 GTEx tissue.	Demonstrate that at least 75% of a consensus list of replicated eQTLs are significant in at least 1 GTEx tissue.	Enroll 300 donors annually.	N/A
CBRR-16 By 2016, demonstrate the use of an efficient, cost-effective pipeline characterizing (phenotype) 2500 genetically modified mice. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: By the end of FY14, produce 1500 knockout lines and phenotype 500 lines. (In Progress)	By the end of FY15, produce 2500 knockout lines and phenotype 1500 lines.	Complete phenotyping the 2500 knockout lines.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
CBRR-17 By FY 2017, take steps to improve the quality and availability of information to inform decisions about the size of the NIH training programs and the number of people in training to address future needs for the nation's biomedical research workforce. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Implement a process to collect information on all graduate students and postdoctorates supported by NIH-funded research projects. (In Progress)	Communicate widely the expectation for grantees to develop an institutional policy requiring Individual Development Plans (IDP) be implemented for every graduate student and post-doctorate supported by any NIH grant, and reportable on the grant progress report.	Implement the collection of information from grantees on career outcomes for graduate students closely associated with training grants.	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. 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)	N/A	N/A	N/A
CTR-2 By 2017, reach 500,000 visits to the website Genome: Unlocking Life's Code. (Outcome)	FY 2015: Result Expected Dec 31, 2015 Target: By 2015, reach 150,000 visits	By 2015, reach 150,000 visits	By 2016, reach an additional 300,000 visits	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
CTR-3 By 2016, partner with 20 state and local mental health nonprofit organizations to facilitate awareness among the general public about the brain, mental health disorders, research-tested interventions and findings, and clinical trials research. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: Partner with 20-25 state and local mental health nonprofit organizations to disseminate science-based information about mental health disorders and research-tested interventions to the general public. (In Progress)	Support 20-25 state and local mental health nonprofit organizations in conducting science-based education and outreach projects addressing the needs of populations that experience mental health disparities as defined by race or ethnicity, age, education or income, disability status, geographic location, and risk status related to sex and gender.	Partner with 20-25 state and local mental health nonprofit organizations to facilitate awareness among the public about the role of basic, translational, and clinical research, and opportunities to participate in clinical research.	N/A
CTR-4 By 2017, expand and implement the broad use of Common Data Elements for 17 neurological disorders among investigators conducting clinical research. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Initiate development of one new set of disease-specific common data elements. (In Progress)	Utilize common data elements in two new clinical trials.	Develop a clinical research training module on utilization of Common Data Elements tools.	N/A
CTR-5 By 2016, increase the number of computer-indexed MEDLINE journals by 288 titles, thereby increasing indexing efficiency for MEDLINE. (Output)	FY 2014: Result Expected Dec 31, 2014 Target: Increase the number of journals indexed automatically by the Medical Text Indexer First Line (MTIFL) process by 96 titles over the previous year.	Increase the number of journals indexed automatically by the Medical Text Indexer First Line (MTIFL) process by 96 titles over the previous year.	Increase the number of journals indexed automatically by the Medical Text Indexer First Line (MTIFL) process by 96 titles over the previous year.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
CTR-6 By FY 2017, improve NIH's ability to identify outcomes that result from NIH funded research projects and report to the public on research outcomes. (Outcome)	FY 2014: Result Expected Dec 31, 2014 Target: By 2014, establish proof-of-concept for a process to link the references cited in published reports about clinical guidelines and practice recommendations to NIH funded research projects. (In Progress)	By 2015, introduce ScienCV, an electronic repository where NIH grant applicants and grantees can gather and store personalized information about their professional accomplishments, and select information from their repository to generate biographical sketches that will be accepted by NIH.	By 2016, establish an electronic closeout process for NIH research grants which includes a Project Outcomes Report for the general public summarizing the project outcomes or findings that expand fundamental knowledge, enhance health, lengthen life, reduce illness and disability, and otherwise fulfill the programmatic goals of the research activity.	N/A
MPO-1 By 2016, decrease by 10% the costs associated with trans-NIH recruitment strategies for intramural research group leaders. (Efficiency)	FY 2014: Result Expected Dec 31, 2014 Target: A 7% decrease in the budget and a minimum of 400 applicants in the combined programs of the Earl Stadtman Investigator search, the Lasker Clinical Research Scholars, and the Early Independent Scientist program. (In Progress)	A 2% decrease in the budget and a minimum of 400 applicants in the combined programs of the Earl Stadtman Investigator search, the Lasker Clinical Research Scholars, and the Early Independent Scientist program.	A 2% decrease in the budget and a minimum of 400 applicants in the combined programs of the Earl Stadtman Investigator search, the Lasker Clinical Research Scholars, and the Early Independent Scientist program.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
MPO-2 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 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)	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 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]	Examine [EX] key area to enhance leadership skills NIH will examine the outcomes of the Executive Leadership Program (ExLP) to determine whether it is effective in meeting its long-term goals, and validate whether the program should continue with its current content [IM 2017/ AS 2018] Implement [IM] recommendation from prior year assessments * 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 [EX 2015 /AS 2017] Assess [AS] results of implementation * Implement recommendations from study of NIH's administrative intern and fellows program [EX 2014/ IM 2015]	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
MPO-3 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-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)	Assess [AS] results of implementation *Create Scientific and Medical Recruitment Forum (SMRF) to attract world-class scientists and medical professionals to drive discovery and innovation at NIH. [IM 2014] 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]	Examine [EX] key area to enhance recruitment *Expansion of the Pathways Program to STEM career path for focused students and supporting of succession planning efforts. [IM 2017] [AS 2018] Implement [IM] 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. [AS 2017] Implement [IM] key area to enhance recruitment *Increase the use of Global Recruitments. [AS 2017]	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
MPO-4 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 access quality of science in order to prioritize resources.	N/A
MPO-5 Improve facility conditions in order to reach and maintain a Condition Index (CI) weighted average of 85 or above (CIwa=85). (Ongoing) (Output and Efficiency)	FY 2013: The condition of the facilities portfolio reached a CIwa of 80.96. Target: CIwa = 75.4 NIH has revised the FY2012 and FY 2013 targets to reflect a change in the way the CI figure is calculated. The new calculation methodology enables NIH to provide consistent results across multiple facility condition reports. Previous target: CIwa = 78.9 (Target Exceeded)	CIwa = 79.9	CIwa = 80.0	N/A
MPO-6 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. (Ongoing) (Output and Efficiency)	FY 2013: 73% of occupied gross square feet (GSF) reached a CI greater than 65. Target: Target = 69.6% (Target Exceeded)	73.5%	Target = 74.0%	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
MPO-7 Manage all Buildings and Facilities (B&F) line item projects so it is completed within 100% of the final approved project cost. (Ongoing) (Output)	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 Previous target: 6 Active Projects (Target Not Met) 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 Previous target: 4 Active Recovery Act projects (Target Met)	11 - Active Projects 1 Active RA Project	5 Active Projects	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
MPO-8 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. (Ongoing) (Output)	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 Previous target: 6 Active Projects (Target Not Met) 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 the approved scope. Target: (2013 RA) 8 Active Recovery Act funded Projects Previous target: 4 Active Recovery Act funded Projects (Target Met)	11 - Active Projects 1 Active RA Project	5 Active Projects	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2015 Target	FY 2016 Target	FY 2016 Target +/-FY 2015 Target
MPO-9 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 2015 OMB/OFPP goal of eligible service contracting dollars to PBC.	Obligate the FY 2016 OMB/OFPP goal of eligible service contracting dollars to PBC.	N/A
MPO-10 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 212 projects are in compliance	N/A	N/A

BUDGET REQUEST BY INSTITUTE AND CENTER

(Dollars in Thousands)	FY 2014 Actual	FY 2015 Enacted[1]	FY 2016 President's Budget
NCI	$4,932,402	$4,953,028	$5,098,479
NHLBI	2,988,584	2,995,865	3,071,906
NIDCR	397,881	397,700	406,746
NIDDK[2]	1,884,486	1,899,140	1,938,133
NINDS	1,588,904	1,604,607	1,660,375
NIAID	4,401,196	4,417,558	4,614,779
NIGMS[3]	2,366,518	2,372,301	2,433,780
NICHD	1,283,338	1,286,869	1,318,061
NEI	675,583	676,764	695,154
NIEHS[4]	743,174	744,682	759,131
NIA	1,171,717	1,197,523	1,267,078
NIAMS	520,355	521,528	533,232
NIDCD	404,284	405,207	416,241
NIMH	1,419,654	1,433,651	1,489,417
NIDA	1,017,961	1,015,705	1,047,397
NIAAA	446,284	447,153	459,833
NINR	140,598	140,852	144,515
NHGRI	498,101	498,677	515,491
NIBIB	327,003	327,243	337,314
NIMHD	268,477	270,969	281,549
NCCIH	124,369	124,062	127,521
NCATS	633,634	632,710	660,131
FIC	67,617	67,634	69,505
NLM[5]	336,613	337,324	394,090
OD	1,303,014	1,413,734	1,442,628
B&F	128,316	128,863	128,863
Total, NIH Program Level	**$30,070,062**	**$30,311,349**	**$31,311,349**
Less funds allocated from different sources:			
Mandatory Type 1 Diabetes Research	-139,200	-150,000	-150,000
PHS Program Evaluation	-8,200	-715,000	-847,489
Total, NIH Discretionary Budget Authority	**$29,922,662**	**$29,446,349**	**$30,313,860**
Interior Budget Authority	-77,349	-77,349	-77,349
Total, NIH Labor/HHS Budget Authority	**$29,845,313**	**$29,369,000**	**$30,236,511**

[1] Excludes Ebola-related funding.

[2] Includes Mandatory Type 1 Diabetes Research funding.

[3] Includes Program Evaluation financing of $715 million in FY 2015 and $847.5 million in FY 2016.

[4] Includes Interior Appropriation for Superfund research.

[5] Includes Program Evaluation financing of $8.2 million in FY 2014.

APPROPRIATIONS ADJUSTMENT TABLE BY INSTITUTE AND CENTER FOR FY 2014

(Dollars in Thousands)	FY 2014 Enacted	1st Sec. Transfers	2nd Sec. Transfers	NCS Transfers	HIV/AIDS Transfers	FY 2014 Final
	FY 2014					
NCI	$4,923,238	-$12,359	-$965	$16,181	6,307	$4,932,402
NHLBI	2,988,605	-7,502	-585	9,822	-1,756	2,988,584
NIDCR	398,650	-1,001	-78	1,310	-1,000	397,881
NIDDK[1]	1,883,474	-4,379	-342	5,733	-	1,884,486
NINDS	1,587,982	-3,986	-311	5,219	-	1,588,904
NIAID	4,358,841	-10,942	-855	14,326	39,826	4,401,196
NIGMS	2,364,147	-5,935	-464	7,770	1,000	2,366,518
NICHD	1,282,595	-3,220	-252	4,215	-	1,283,338
NEI	682,077	-1,712	-134	2,242	-6,890	675,583
NIEHS[2]	742,788	-1,670	-131	2,187	-	743,174
NIA	1,171,038	-2,940	-230	3,849	-	1,171,717
NIAMS	520,053	-1,305	-102	1,709	-	520,355
NIDCD	404,049	-1,014	-79	1,328	-	404,284
NIMH	1,446,172	-3,630	-284	4,753	-27,357	1,419,654
NIDA	1,025,435	-2,574	-	3,370	-8,270	1,017,961
NIAAA	446,025	-1,120	-87	1,466	-	446,284
NINR	140,517	-353	-28	462	-	140,598
NHGRI	497,813	-1,250	-98	1,636	-	498,101
NIBIB	329,172	-826	-65	1,082	-2,360	327,003
NIMHD	268,322	-674	-53	882	-	268,477
NCCIH	124,296	-312	-24	409	-	124,369
NCATS	633,267	-1,590	-124	2,081	-	633,634
FIC	67,577	-169	-13	222	-	67,617
NLM[3]	335,923	-823	-64	1,077	500	336,613
OD	1,400,134	-3,515	-275	-93,330	-	1,303,014
B&F	128,663	-322	-25	-	-	128,316
Total, NIH Program Level	**$30,150,853**	**-$75,123**	**-$5,668**	-	-	**$30,070,062**
Less funds allocated from different sources:						
Mandatory Type 1 Diabetes Research	-139,200					-139,200
PHS Program Evaluation	-8,200					-8,200
Total, NIH Discretionary Budget Authority	**$30,003,453**	**-$75,123**	**-$5,668**	-	-	**$29,922,662**
Interior Budget Authority	-77,349					-77,349
Total, NIH Labor/HHS Budget Authority	**$29,926,104**	**-$75,123**	**-$5,668**	-	-	**$29,845,313**

[1] Includes Mandatory Type 1 Diabetes Research funding.

[2] Includes Interior Appropriation for Superfund research.

[3] Includes Program Evaluation financing of $8.2 million in FY 2014.

APPROPRIATIONS ADJUSTMENT TABLE BY INSTITUTE AND CENTER FOR FY 2015

FY 2015			
(Dollars in Thousands)	**FY 2015 Enacted[1]**	**HIV/AIDS Transfers**	**FY 2015 Operating Level**
NCI	$4,950,396	$2,632	$4,953,028
NHLBI	2,997,870	-2,005	2,995,865
NIDCR	399,886	-2,186	397,700
NIDDK[2]	1,899,681	-541	1,899,140
NINDS	1,605,205	-598	1,604,607
NIAID	4,358,841	58,717	4,417,558
NIGMS[3]	2,371,476	825	2,372,301
NICHD	1,286,571	298	1,286,869
NEI	684,191	-7,427	676,764
NIEHS[4]	744,851	-169	744,682
NIA	1,199,468	-1,945	1,197,523
NIAMS	521,665	-137	521,528
NIDCD	405,302	-95	405,207
NIMH	1,463,036	-29,385	1,433,651
NIDA	1,028,614	-12,909	1,015,705
NIAAA	447,408	-255	447,153
NINR	140,953	-101	140,852
NHGRI	499,356	-679	498,677
NIBIB	330,192	-2,949	327,243
NIMHD	269,154	1,815	270,969
NCCIH	124,681	-619	124,062
NCATS	635,230	-2,520	632,710
FIC	67,786	-152	67,634
NLM	336,939	385	337,324
OD	1,413,734	-	1,413,734
B&F	128,863	-	128,863
Total, NIH Program Level	**$30,311,349**	-	**$30,311,349**
Less funds allocated from different sources:			
Mandatory Type 1 Diabetes Research	-150,000		-150,000
PHS Program Evaluation	-715,000		-715,000
Total, NIH Discretionary Budget Authority	**$29,446,349**	-	**$29,446,349**
Interior Budget Authority	-77,349		-77,349
Total, NIH Labor/HHS Budget Authority	**$29,369,000**	-	**$29,369,000**

[1] Excludes Ebola-related funding.

[2] Includes Mandatory Type 1 Diabetes Research funding.

[3] Includes Program Evaluation financing of $715 million.

[4] Includes Interior Appropriation for Superfund research.

BUDGET MECHANISM TABLE

(Dollars in Thousands) [1, 2]	FY 2014 Actual		FY 2015 Enacted[7]		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	23,504	$10,785,361	23,433	$11,294,016	23,303	$11,524,971	-130	$230,955
Administrative Supplements	*(1,588)*	208,245	*(1,479)*	172,045	*(1,420)*	168,834	*(-59)*	-3,212
Competing:								
Renewal	1,897	1,297,091	2,049	1,062,346	2,264	1,143,837	215	81,491
New	7,223	3,167,751	6,987	3,078,440	7,996	3,592,077	1,009	513,637
Supplements	48	14,318	40	9,781	43	10,641	3	859
Subtotal, Competing	9,168	$4,479,160	9,076	$4,150,567	10,303	$4,746,555	1,227	$595,988
Subtotal, RPGs	32,672	$15,472,767	32,509	$15,616,627	33,606	$16,440,359	1,097	$823,732
SBIR/STTR	1,660	695,480	1,697	716,012	1,841	765,300	144	49,288
Research Project Grants	34,332	$16,168,247	34,206	$16,332,639	35,447	$17,205,659	1,241	$873,020
Research Centers:								
Specialized/Comprehensive	1,117	$1,958,143	1,130	$1,929,147	1,171	$1,894,298	41	-$34,849
Clinical Research	60	413,671	60	416,824	60	411,742		-5,082
Biotechnology	93	167,045	94	165,694	99	152,972	5	-12,722
Comparative Medicine	51	129,353	52	131,500	49	122,254	-3	-9,246
Research Centers in Minority Institutions	22	55,067	21	56,127	20	55,377	-1	-750
Research Centers	1,343	$2,723,280	1,357	$2,699,292	1,399	$2,636,643	42	-$62,650
Other Research:								
Research Careers	3,624	$611,866	3,632	$614,794	3,648	$619,919	16	$5,125
Cancer Education	96	32,932	96	32,932	96	32,738		-195
Cooperative Clinical Research	394	474,587	385	468,828	386	503,987	1	35,160
Biomedical Research Support	111	67,391	105	64,579	105	64,579		
Minority Biomedical Research Support	287	104,470	283	103,115	282	102,920	-1	-195
Other	1,722	555,627	1,689	559,959	2,010	557,907	321	-2,053
Other Research	6,234	$1,846,873	6,190	$1,844,207	6,527	$1,882,049	337	$37,842
Total Research Grants	41,909	$20,738,399	41,753	$20,876,138	43,373	$21,724,351	1,620	$848,213
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,058	$136,141	3,105	$140,036	3,234	$146,846	129	$6,810
Institutional Awards	12,258	602,287	12,426	622,034	12,501	638,636	75	16,602
Total Research Training	15,316	$738,429	15,531	$762,071	15,735	$785,483	204	$23,412
Research & Develop. Contracts	2,211	$2,990,140	2,078	$2,898,740	2,095	$2,895,964	17	-$2,777
(SBIR/STTR) (non-add)	*(115)*	*(65,426)*	*(129)*	*(73,771)*	*(132)*	*(78,580)*	*(3)*	*(4,810)*
Intramural Research	7,060	$3,384,285	7,087	$3,425,860	7,080	$3,520,574	-7	$94,714
Res. Management & Support	5,574	1,527,790	5,624	1,560,897	5,631	1,580,442	7	19,544
(SBIR Administrative) (non-add)	*(3)*	*(3,687)*	*(30)*	*(4,054)*	*(0)*	*(0)*	*(-30)*	*(-4,054)*
Office of the Director - Appropriation [3]		*(1,303,014)*		*(1,413,734)*		*(1,442,628)*		*(28,894)*
Office of the Director - Other		477,354		573,430		582,324		8,894
ORIP/SEPA (non-add) [3]		*(294,486)*		*(294,665)*		*(294,665)*		*(0)*
Common Fund (non-add) [3]		*(531,174)*		*(545,639)*		*(565,639)*		*(20,000)*
Buildings and Facilities[4]		136,316		136,863		144,863		8,000
Appropriation		*(128,663)*		*(128,863)*		*(128,863)*		*(0)*
Type 1 Diabetes[5]		-139,200		-150,000		-150,000		0
Program Evaluation Financing[6]		-8,200		-715,000		-847,489		-132,489
Subtotal, Labor/HHS Budget Authority		**$29,845,313**		**$29,369,000**		**$30,236,511**		**$867,511**
Interior Appropriation for Superfund Research		77,349		77,349		77,349		0
Total, NIH Discretionary Budget Authority		**$29,922,662**		**$29,446,349**		**$30,313,860**		**$867,511**
Type 1 Diabetes		139,200		150,000		150,000		0
Total, NIH Budget Authority		**$30,061,862**		**$29,596,349**		**$30,463,860**		**$867,511**
Program Evaluation Financing		8,200		715,000		847,489		132,489
Total, Program Level		**$30,070,062**		**$30,311,349**		**$31,311,349**		**$1,000,000**

[1] All Subtotal and Total numbers may not add due to rounding.
[2] All numbers in italics and brackets are non-add.
[3] Number of grants and dollars for the Common Fund, ORIP and SEPA components of OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriations also is noted as a non-add since the remaining funds are accounted
[4] Includes B&F appropriation and funds for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
[5] 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.
[6] Number of grants and dollars for Program Evaluation Financing are distributed by mechanism above; therefore, the amount is deducted to provide subtotals only for the Labor/HHS Budget Authority.
[7] Excludes Ebola related funding.

BUDGET AUTHORITY BY OBJECT CLASSIFICATION INCLUDING TYPE 1 DIABETES

(Dollars in Thousands)[1]	FY 2015 Enacted[2]	FY 2016 President's Budget	FY 2016 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$922,092	$939,186	$17,094
Other Than Full-Time Permanent (11.3)	460,980	498,469	37,489
Other Personnel Compensation (11.5)	33,913	34,444	531
Military Personnel (11.7)	19,915	20,204	289
Special Personnel Services Payments (11.8)	158,223	160,516	2,293
Subtotal Personnel Compensation (11.9)	**$1,595,122**	**$1,652,819**	**$57,697**
Civilian Personnel Benefits (12.1)	441,255	458,505	17,250
Military Personnel Benefits (12.2)	14,230	14,520	290
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,050,607**	**$2,125,479**	**$74,872**
Travel & Transportation of Persons (21.0)	45,114	45,646	533
Transportation of Things (22.0)	5,248	5,311	63
Rental Payments to GSA (23.1)	14,481	14,712	231
Rental Payments to Others (23.2)	368	374	6
Communications, Utilities & Misc. Charges (23.3)	24,256	24,514	258
Printing & Reproduction (24.0)	594	605	12
Consultant Services (25.1)	168,356	164,551	-3,805
Other Services (25.2)	893,749	871,992	-21,758
Purchase of goods and services from government accounts (25.3)	3,009,190	3,191,655	182,465
Operation & Maintenance of Facilities (25.4)	173,345	173,425	80
R&D Contracts (25.5)	1,691,410	1,626,258	-65,152
Medical Care (25.6)	27,873	28,422	549
Operation & Maintenance of Equipment (25.7)	104,741	105,760	1,019
Subsistence & Support of Persons (25.8)	8	8	0
Subtotal Other Contractual Services (25.0)	**$6,068,673**	**$6,162,071**	**$93,398**
Supplies & Materials (26.0)	178,436	179,644	1,208
Equipment (31.0)	154,292	154,883	591
Land and Structures (32.0)	0	1	0
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	21,691,919	22,520,384	828,466
Insurance Claims & Indemnities (42.0)	2	2	0
Interest & Dividends (43.0)	9	9	0
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$28,183,393**	**$29,108,156**	**$924,763**
Total Budget Authority	**$30,234,000**	**$31,234,000**	**$1,000,000**

[1] Excludes Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee.

[2] Excludes Ebola-related funding.

BUDGET AUTHORITY BY OBJECT CLASSIFICATION INCLUDING SERVICE AND SUPPLY FUND AND MANAGEMENT FUND

(Dollars in Thousands)[1]	FY 2015 Enacted[2]	FY 2016 President's Budget	FY 2016 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$1,263,835	$1,289,473	$25,638
Other Than Full-Time Permanent (11.3)	541,734	580,838	39,104
Other Personnel Compensation (11.5)	56,303	57,192	889
Military Personnel (11.7)	28,826	29,222	396
Special Personnel Services Payments (11.8)	163,680	166,027	2,348
Subtotal Personnel Compensation (11.9)	**$2,054,377**	**$2,122,753**	**$68,375**
Civilian Personnel Benefits (12.1)	561,827	580,765	18,938
Military Personnel Benefits (12.2)	20,811	21,180	369
Benefits to Former Personnel (13.0)	1,912	1,914	2
Total Pay Costs	**$2,638,927**	**$2,726,247**	**$87,320**
Travel & Transportation of Persons (21.0)	47,218	47,771	554
Transportation of Things (22.0)	6,793	6,871	78
Rental Payments to GSA (23.1)	67,190	68,212	1,021
Rental Payments to Others (23.2)	90,551	91,639	1,088
Communications, Utilities & Misc. Charges (23.3)	150,016	151,531	1,515
Printing & Reproduction (24.0)	1,018	1,034	16
Consultant Services (25.1)	309,929	310,655	726
Other Services (25.2)	1,266,376	1,252,983	-13,393
Purchase of goods and services from government accounts (25.3)	1,228,400	1,374,395	145,995
Operation & Maintenance of Facilities (25.4)	265,489	268,793	3,305
R&D Contracts (25.5)	1,691,648	1,626,502	-65,146
Medical Care (25.6)	33,420	34,107	688
Operation & Maintenance of Equipment (25.7)	247,068	248,541	1,473
Subsistence & Support of Persons (25.8)	8	8	0
Subtotal Other Contractual Services (25.0)	**$5,042,338**	**$5,115,986**	**$73,648**
Supplies & Materials (26.0)	294,290	298,394	4,104
Equipment (31.0)	203,676	205,501	1,825
Land and Structures (32.0)	1	1	0
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	21,691,919	22,520,384	828,466
Insurance Claims & Indemnities (42.0)	3	3	0
Interest & Dividends (43.0)	61	62	1
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$27,595,073**	**$28,507,389**	**$912,316**
Total Budget Authority	**$30,234,000**	**$31,234,000**	**$1,000,000**

[1] Excludes Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee.

[2] Excludes Ebola-related funding.

SALARIES AND EXPENSES

Object Classes Including Type I Diabetes Funds[1] (Dollars in Thoudands)	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$922,092	$939,186	$17,094
Other Than Full-Time Permanent (11.3)	460,980	498,469	37,489
Other Personnel Compensation (11.5)	33,913	34,444	531
Military Personnel (11.7)	19,915	20,204	289
Special Personnel Services Payments (11.8)	158,223	160,516	2,293
Subtotal Personnel Compensation (11.9)	**$1,595,122**	**$1,652,819**	**$57,697**
Civilian Personnel Benefits (12.1)	441,255	458,505	17,250
Military Personnel Benefits (12.2)	14,230	14,520	290
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,050,607**	**$2,125,479**	**$74,872**
Travel & Transportation of Persons (21.0)	45,114	45,646	533
Transportation of Things (22.0)	5,248	5,311	63
Rental Payments to Others (23.2)	368	374	6
Communications, Utilities & Misc. Charges (23.3)	24,256	24,514	258
Printing & Reproduction (24.0)	594	605	12
Other Contractual Services:			
Consultant Services (25.1)	141,410	143,528	2,118
Other Services (25.2)	893,749	871,992	-21,758
Purchase of goods and services from government accounts (25.3)[2]	1,959,453	2,005,664	46,211
Operation & Maintenance of Facilities (25.4)	165,337	165,288	-49
Operation & Maintenance of Equipment (25.7)	104,741	105,760	1,019
Subsistence & Support of Persons (25.8)	8	8	0
Subtotal Other Contractual Services	**$3,264,699**	**$3,292,241**	**$27,542**
Supplies & Materials (26.0)	178,436	179,644	1,208
Subtotal Non-Pay Costs	**$3,518,715**	**$3,548,335**	**$29,620**
Total Salaries and Expense / Administrative Costs	**$5,569,322**	**$5,674,179**	**$104,857**
Direct FTE	**13,351**	**13,351**	**0**

[1] Excludes Superfund Research account under the jurisdiction of the Interior, Environment & Related Agencies Appropriations Subcommittee.
[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.

DETAIL OF FULL-TIME EQUIVALENT EMPLOYMENT (FTE)

Institutes and Centers (ICs)	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
NCI	3,040	3,057	3,057
NHLBI	927	932	932
NIDCR	238	239	239
NIDDK	628	632	632
NINDS	532	535	535
NIAID	1,972	1,983	1,983
NIGMS	185	186	186
NICHD	564	567	567
NEI	261	262	262
NIEHS	657	661	661
NIA	392	394	394
NIAMS	242	243	243
NIDCD	139	140	140
NIMH	555	558	558
NIDA	393	395	395
NIAAA	236	237	237
NINR	91	92	92
NHGRI	330	332	332
NIBIB	101	102	102
NCATS	125	126	126
NCCIH	75	76	76
NIMHD	66	66	66
FIC	63	63	63
NLM	799	804	804
OD	664	669	669
Central Services [1]	4,773	4,799	4,799
Total	**18,048**	**18,150**	**18,150**
PHS Trust Fund (non-add) [2]	*4*	*4*	*4*
CRADA (non-add) [3]	*5*	*5*	*5*
Grand Total	**18,048**	**18,150**	**18,150**

[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 incorporated within the IC's Direct-funded civilian FTE category and are treated as non-add values.

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

HISTORY OF OBLIGATIONS BY INSTITUTE AND CENTER

(Dollars in Thousands)	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 2014 Actual Obligations	FY 2015 Enacted[1]	FY 2016 President's Budget
NCI	$4,792,615	$4,827,552	$4,966,927	$5,098,147	$5,058,105	5,062,763	4,789,014	$4,932,368	$4,953,028	$5,098,479
NHLBI	2,922,323	2,937,333	3,014,552	3,093,501	3,069,550	3,073,302	2,903,768	2,988,415	2,995,865	3,071,906
NIDCR	389,060	391,136	402,011	412,527	409,549	409,947	387,309	397,833	397,700	406,746
NIDDK[2]	1,852,990	1,862,188	1,911,795	1,958,905	1,942,155	1,943,706	1,837,027	1,884,377	1,899,140	1,938,133
NINDS	1,532,977	1,549,543	1,590,781	1,633,568	1,622,001	1,623,344	1,533,793	1,588,899	1,604,607	1,660,375
NIAID	4,264,034	4,286,410	4,400,398	4,515,426	4,478,595	4,482,369	4,235,094	4,401,185	4,417,558	4,614,779
NIGMS[3]	1,932,481	1,942,783	1,994,426	2,048,112	2,033,663	2,425,522	2,293,044	2,366,429	2,372,301	2,433,780
NICHD	1,252,765	1,259,435	1,292,929	1,327,349	1,317,682	1,318,943	1,246,140	1,283,314	1,286,869	1,318,061
NEI	665,863	669,534	687,350	705,792	700,781	701,407	657,055	675,551	676,764	695,154
NIEHS[4]	726,131	729,088	746,107	774,008	762,602	763,225	721,331	743,002	744,682	759,131
NIA	1,045,468	1,050,998	1,079,004	1,108,208	1,100,445	1,120,391	1,040,565	1,171,656	1,197,523	1,267,078
NIAMS	507,292	510,358	523,887	538,028	534,260	534,791	505,206	520,314	521,528	533,232
NIDCD	392,937	395,515	406,516	418,001	415,104	415,500	392,540	404,237	405,207	416,241
NIMH	1,402,385	1,414,541	1,454,377	1,493,510	1,477,257	1,477,516	1,396,006	1,419,632	1,433,651	1,489,417
NIDA	1,001,952	1,007,295	1,039,561	1,066,909	1,050,519	1,051,410	993,404	1,017,957	1,015,705	1,047,397
NIAAA	435,366	437,839	449,524	461,544	458,257	458,665	433,247	446,282	447,153	459,833
NINR	137,167	137,990	141,660	145,420	144,369	144,500	136,516	140,553	140,852	144,515
NHGRI	508,240	505,380	507,210	524,131	511,469	512,258	483,650	498,076	498,677	515,491
NIBIB	296,380	299,726	307,701	316,028	313,787	337,728	319,062	326,989	327,243	337,314
NIMHD	199,083	200,252	205,616	211,194	209,693	275,927	260,671	268,439	270,969	281,549
NCRR	1,131,618	1,153,911	1,224,629	1,267,021	1,257,641	---	---	---	---	---
NCCAM	121,369	122,013	125,265	128,615	127,706	127,820	120,767	124,368	124,062	127,521
NCATS	---	---	---	---	---	574,297	542,598	633,571	632,710	660,131
FIC	66,348	66,828	68,607	69,957	69,413	69,493	65,627	67,575	67,634	69,505
NLM[5]	329,554	331,585	337,814	348,467	344,860	373,087	325,088	334,383	337,324	394,090
ORIP & SEPA	---	---	---	---	---	303,525	290,042	294,486	294,665	294,665
Common Fund	482,961	498,240	541,133	544,028	543,017	544,930	513,461	531,146	545,639	565,639
OD - Other	563,596	613,454	706,295	632,966	623,887	608,713	608,584	477,293	573,430	582,324
B&F	89,114	127,227	88,815	203,056	62,161	125,308	106,676	88,880	128,863	128,863
Total, NIH Program Level	**$29,042,069**	**$29,328,154**	**$30,214,890**	**$31,044,418**	**$30,638,528**	**30,860,387**	**$29,137,284**	**$30,027,205**	**$30,311,349**	**$31,311,349**
Less funds allocated from different sources:										
Mandatory Type 1 Diabetes Research	-150,000	-150,000	-150,000	-150,000	-150,000	-150,000	-142,350	-139,200	-150,000	-150,000
PHS Program Evaluation	-8,200	-8,200	-8,200	-8,200	-8,200	-8,200	-8,200	-8,200	-715,000	-847,489
Total, NIH Discretionary Budget Authority	**28,883,869**	**29,169,954**	**30,056,690**	**30,886,218**	**30,480,328**	**30,702,187**	**28,986,734**	**29,879,805**	**29,446,349**	**30,313,860**
Interior Budget Authority	-79,111	-77,531	-78,070	-79,201	-79,045	-78,928	-74,864	-77,345	-77,349	-77,349
Total, NIH Labor/HHS Budget Authority	**28,804,758**	**29,092,423**	**29,978,620**	**30,807,017**	**30,401,283**	**30,623,259**	**28,911,870**	**29,802,460**	**29,369,000**	**30,236,511**

[1] Excludes Ebola-related funding.

[2] Includes Mandatory Type 1 Diabetes Research funding.

[3] Includes Program Evaluation financng of $715 million for FY 2015 and $847.5 million for FY 2016.

[4] Includes Interior Appropriation for Superfund research.

[5] Includes Program Evaluation financing of $8.2 million except in FY 2015 and FY 2016.

HISTORY OF OBLIGATIONS BY TOTAL MECHANISM

(Dollars in Thousands)[1]	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 2014 Actual Obligations	FY 2015 Enacted[4, 5]	FY 2016 President's Budget
Res. Project Grants	$15,333,540	$15,688,339	$16,124,554	$16,501,300	$16,428,047	$16,550,486	$15,445,463	$16,168,246	$16,332,639	$17,205,659
Research Centers	2,709,259	2,946,346	3,018,710	3,082,914	3,009,480	3,040,375	$2,708,744	2,723,203	2,699,292	2,636,643
Other Research	1,652,501	1,779,990	1,775,387	1,794,148	1,802,937	1,808,138	$1,783,481	1,846,841	1,844,207	1,882,049
Subtotal, Res. Grants	$19,695,300	$20,414,675	$20,918,651	$21,378,362	$21,240,464	$21,398,999	$19,937,688	$20,738,290	$20,876,138	$21,724,351
Research Training	763,797	770,480	776,193	775,186	771,766	761,934	$733,524	738,429	762,071	785,483
R & D Contracts	2,693,443	2,934,858	3,069,412	3,143,929	2,996,640	2,937,188	$2,927,077	2,990,037	2,898,740	2,895,964
Intramural Research	3,002,558	3,091,240	3,222,852	3,306,312	3,330,815	3,401,506	$3,247,193	3,373,601	3,425,860	3,520,574
Res. Mgt. & Support	1,136,197	1,372,225	1,428,138	1,509,287	1,517,630	1,530,874	$1,485,575	1,527,131	1,560,897	1,580,442
Cancer Control[2]	498,396	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Construction	14,100	0	0	0	0	0	$0	0	0	0
Library of Medicine[2]	7,376	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Office of the Director	1,046,557	523,798	616,639	632,966	623,887	609,530	$608,584	477,293	573,430	582,324
Subtotal	**$28,857,724**	**$29,107,276**	**$30,031,885**	**$30,746,042**	**$30,481,202**	**$30,640,031**	**$28,939,641**	**$29,844,781**	**$30,097,137**	**$31,089,137**
Buildings & Facilities[3]	97,034	135,147	96,735	210,975	70,081	133,228	$114,580	96,880	136,863	144,863
Interior- Superfund	79,111	77,531	78,070	79,201	79,045	78,928	$74,864	77,345	77,349	77,349
Total, NIH Budget Authority	**$29,033,869**	**$29,319,954**	**$30,206,690**	**$31,036,218**	**$30,630,328**	**$30,852,187**	**$29,129,085**	**$30,019,005**	**$30,311,349**	**$31,311,349**

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

[2] 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.

[3] 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.

[4] Includes HIV/AIDS transfers.

[5] Excludes Ebola related funding.

PROGRAMS PROPOSED FOR ELIMINATION

The FY 2016 Budget continues to propose a 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, one NIH STEM program will be eliminated in FY 2016. The following table shows the program proposed for elimination or consolidation in the FY 2016 President's Budget request.

Program	FY 2015
NINDS Diversity Research Education Grants in Neuroscience	$1,000,000

Rationale

STEM Programs (-$1.0 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.

PHYSICIANS' COMPARABILITY ALLOWANCE WORKSHEET

		FY 2014 Actual	FY 2015 Enacted	FY 2016 * President's Budget
1) Number of Physicians Receiving PCAs		161	161	161
2) Number of Physicians with One-Year PCA		11	11	11
3) Number of Physicians with Multi-Year PCA		150	150	150
4) Average Annual PCA Physician Pay (without PCA payment)		$149,775	$151,273	$152,786
5) Average Annual PCA Payment		$12,860	$12,989	$13,119
6) Number of Physicians Receiving PCAs by Category (non-add)	Category I Clinical Position			
	Category II Research Position	160	160	160
	Category III Occupational Health			
	Category IV-A Disability Evaluation			
	Category IV-B Health and Medical Admin.	1	1	1

* FY 2016 data will be approved during the FY 2017 Budget cycle.

7) If applicable, list and explain the necessity of any addition 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 vary based on grade level and amount of federal service. The monetary range is between $10,000 and $30,000. These flexible amounts are necessary to recruit and 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 strives to make progress recruiting and retaining qualified physicians to the Federal service. However, due to competition and more lucrative compensation in the private sector it continues to be challenging. NIH has had a historically high turnover rate for physicians. NIH physicians require unique and specialized qualifications that make it often difficult to fill positions when vacated.

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 2014, there was a total of 161 PCA recipients across NIH. In FY 2015 and beyond, a critical need will continue to exist for highly qualified, specialized physicians to support the NIH mission. NIH still requires compensation flexibilities such as PCA to attract and retain qualified physicians. Aggressive recruitment efforts were able to substantially mitigate turnover of 3.7% in 2014, which was more moderate than anticipated but is not expected to recur in the future. There were 7 accessions offsetting 6 separations.

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

N/A

STATISTICAL DATA: DIRECT AND INDIRECT COSTS AWARDED

(Dollars in Thousands)	Direct Cost Awarded	Indirect Cost Awarded	Percent of Total		Percent Change	
			Direct Cost Awarded	Indirect Cost Awarded	Direct Cost Awarded	Indirect Cost Awarded
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	$15,568,553	$5,908,275	72.5%	27.5%	4.4%	2.7%
FY 2015 Enacted	$15,685,538	$5,952,671	72.5%	27.5%	5.2%	3.4%
FY 2016 President's Budget	$16,317,379	$6,192,455	72.5%	27.5%	4.0%	4.0%

Note: FY 2015 and FY 2016 data represent estimates and will change as actual data is received.

RESEARCH PROJECT GRANTS: TOTAL NUMBER OF AWARDS AND FUNDING

(Dollars in Thousands)	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015 Enacted[1]	FY 2016 PB Request[1]
No. of Awards:										
Competing	10,323	9,714	9,121	9,386	8,706	8,986	8,234	9,168	9,076	10,303
Noncompeting	26,741	26,610	26,217	25,738	26,166	25,631	25,140	23,504	23,433	23,303
Subtotal	37,064	36,324	35,338	35,124	34,872	34,617	33,374	32,672	32,509	33,606
SBIR/STTR	1,781	1,838	1,740	1,685	1,494	1,642	1,466	1,660	1,697	1,841
Total	**38,845**	**38,162**	**37,078**	**36,809**	**36,366**	**36,259**	**34,840**	**34,332**	**34,206**	**35,447**
Average Annual Cost:										
Competing	$367	$377	$427	$417	$427	$421	$418	$489	$457	$461
Total RPGs	$405	$414	$438	$450	$453	$459	$444	$474	$480	$489
Percent Change over prior year Average Costs:										
Competing RPGs	-0.3%	2.8%	13.2%	-2.4%	2.5%	-1.5%	-0.8%	17.0%	-6.4%	0.7%
Total RPGs[2]	0.4%	2.2%	5.8%	3.0%	0.5%	1.4%	-3.3%	6.7%	1.4%	1.8%
Average Length[3] of Award in Years	3.8	3.8	3.8	3.8	3.7	3.5	3.5	3.5	3.5	3.5

[1] Numbers of grants identified in the FY 2015 and the FY 2016 are estimates, and will change as applications are received and selected for funding.

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

[3] Durations are estimated for FY 2015 and FY 2016 based on FY 2014 grant award results.

RESEARCH PROJECT GRANTS: SUCCESS RATES

INSTITUTES & CENTERS * [1,2]	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015 Enacted	FY 2016 PB	INSTITUTES & CENTERS
NCI	20.1%	21.0%	19.0%	17.1%	13.8%	13.6%	13.7%	14.1%	12.3%	13.7%	NCI
NHLBI	21.0%	22.0%	22.0%	19.9%	17.4%	14.7%	16.9%	18.2%	18.6%	25.3%	NHLBI
NIDCR	22.4%	20.0%	19.0%	22.2%	22.5%	21.2%	19.9%	21.5%	20.6%	18.5%	NIDCR
NIDDK	20.9%	25.0%	23.0%	25.9%	20.7%	19.8%	21.0%	22.9%	22.1%	23.2%	NIDDK
NINDS	18.7%	21.0%	21.0%	22.6%	21.1%	19.5%	19.8%	18.7%	17.9%	21.1%	NINDS
NIAID	23.0%	23.0%	19.0%	23.9%	20.2%	23.2%	18.8%	22.0%	21.6%	24.6%	NIAID
NIGMS	32.1%	27.0%	27.0%	26.9%	23.1%	24.4%	19.9%	24.8%	25.7%	25.4%	NIGMS
NICHD	20.6%	17.0%	15.0%	15.2%	12.4%	12.5%	10.8%	12.5%	10.8%	13.6%	NICHD
NEI	26.6%	30.0%	30.0%	26.9%	28.8%	29.8%	23.7%	26.7%	21.9%	25.7%	NEI
NIEHS	18.5%	18.0%	18.0%	25.1%	14.7%	14.3%	15.3%	15.0%	14.5%	16.7%	NIEHS
NIA	22.1%	20.0%	18.0%	14.5%	16.1%	15.5%	13.6%	15.9%	14.6%	15.1%	NIA
NIAMS	20.0%	21.0%	20.0%	21.4%	14.9%	15.6%	15.9%	18.1%	19.1%	19.7%	NIAMS
NIDCD	31.0%	29.0%	32.0%	30.2%	27.5%	26.6%	22.5%	25.8%	24.4%	26.6%	NIDCD
NIMH	22.1%	21.0%	22.0%	22.1%	17.1%	21.6%	18.7%	19.4%	18.3%	19.8%	NIMH
NIDA	23.4%	24.0%	22.0%	19.8%	18.2%	21.2%	19.5%	18.0%	15.2%	15.8%	NIDA
NIAAA	27.2%	26.0%	24.0%	26.5%	18.6%	18.4%	19.5%	19.2%	16.6%	19.1%	NIAAA
NINR	25.6%	20.0%	21.0%	13.2%	8.5%	13.0%	9.1%	11.6%	9.1%	10.4%	NINR
NHGRI	28.0%	32.0%	34.0%	33.6%	27.4%	23.9%	20.5%	17.7%	19.1%	18.9%	NHGRI
NIBIB	21.5%	19.0%	18.0%	16.0%	12.9%	12.1%	13.7%	13.1%	12.2%	16.1%	NIBIB
NIMHD[3]	N/A	N/A	11.0%	8.0%	11.9%	9.9%	4.3%	11.9%	18.2%	34.8%	NIMHD
NCCIH[4]	10.8%	12.0%	12.0%	11.0%	9.1%	9.5%	11.6%	8.7%	9.1%	10.3%	NCCIH
NCATS[5]	N/A	N/A	N/A	N/A	N/A	0.0%	0.0%	16.7%	10.0%	0.0%	NCATS
FIC	25.1%	28.0%	21.0%	26.1%	11.9%	16.0%	14.6%	9.1%	18.2%	45.2%	FIC
NLM	18.7%	21.0%	12.0%	21.1%	16.1%	12.8%	12.3%	19.4%	25.3%	31.6%	NLM
ORIP & SEPA[6]	20.3%	15.0%	22.0%	22.0%	21.3%	18.6%	20.0%	19.6%	34.5%	39.7%	ORIP & SEPA
Common Fund	7.0%	12.0%	17.0%	11.1%	11.3%	8.0%	9.2%	10.0%	9.9%	9.4%	Common Fund
NIH[7]	**20.0%**	**21.3%**	**21.0%**	**21.0%**	**20.5%**	**17.5%**	**16.7%**	**18.0%**	**17.2%**	**19.3%**	**NIH**

* Success Rates identified in FY 2015 and FY 2016 are estimates, and will change as applications are received and selected for funding.

[1] Includes Special type 1 Diabetes 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] 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.

[4] The National Center for Complementary and Alternative Medicine (NCCAM) was renamed in December 2014 to the National Center for Complementary and Integrative Health (NCCIH) consistent with enactment of the Consolidated and Further Continuing Appropriations Act, 2015 (P.L. 113-235).

[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] 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.

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

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.

Budget Authority by Activity*
(Dollars in Thousands)

Detail	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget	
	FTE	Amount	FTE	Amount	FTE	Amount
Clinical Center	1,873	$424,321	1,884	$428,564	1,884	$439,278
Center for Scientific Review, SREA	375	109,274	377	110,367	377	113,126
Research Support and Adminstrative Services, OD	69	29,158	69	29,450	69	30,186
Office of Research Services, Facilities, Development & Operations	588	87,449	587	88,323	587	90,532
TOTAL	**2,905**	**$650,202**	**2,917**	**$656,704**	**2,917**	**$673,122**

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

Budget Authority by Object Class*

(Dollars in Thousands)

		FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Total compensable workyears:				
	Full-time employment	2,917	2,917	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$179	$180	$1
	Average GM/GS grade	11.7	11.7	0.0
	Average GM/GS salary	$95	$96	$1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$83	$84	$0
	Average salary of ungraded positions	$127	$131	$0
	OBJECT CLASSES	**FY 2015 Enacted**	**FY 2016 President's Budget**	**FY 2016 +/- FY 2015**
	Personnel Compensation			
11.1	Full-Time Permanent	$162,297	$166,354	$4,057
11.3	Other Than Full-Time Permanent	70,895	72,313	1,418
11.5	Other Personnel Compensation	13,976	14,200	224
11.7	Military Personnel	6,581	6,660	79
11.8	Special Personnel Services Payments	4,787	4,835	48
11.9	**Subtotal Personnel Compensation**	**$258,536**	**$264,362**	**$5,826**
12.1	Civilian Personnel Benefits	$70,844	$71,836	$992
12.2	Military Personnel Benefits	5,343	5,407	64
13.0	Benefits to Former Personnel	200	202	2
	Subtotal Pay Costs	**$334,923**	**$341,807**	**$6,884**
21.0	Travel & Transportation of Persons	$1,598	$1,614	$16
22.0	Transportation of Things	702	709	7
23.1	Rental Payments to GSA	15	15	0
23.2	Rental Payments to Others	5	5	0
23.3	Communications, Utilities & Misc. Charges	5,029	5,080	50
24.0	Printing & Reproduction	407	411	4
25.1	Consulting Services	$10,780	$11,125	$345
25.2	Other Services	91,187	93,923	2,736
25.3	Purchase of goods and services from government accounts	93,091	96,438	3,347
25.4	Operation & Maintenance of Facilities	$17,256	$17,860	$604
25.5	R&D Contracts	125	128	3
25.6	Medical Care	4,996	5,120	125
25.7	Operation & Maintenance of Equipment	13,791	14,018	227
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$231,225**	**$238,612**	**$7,386**
26.0	Supplies & Materials	$66,405	$68,066	$1,660
31.0	Equipment	16,387	16,797	410
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	0	0	0
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	7	7	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$321,781**	**$331,315**	**$9,534**
	Total Budget Authority by Object Class	**$656,704**	**$673,122**	**$16,418**

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

Detail of Positions*

GRADE	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Total, ES Positions	5	5	5
Total, ES Salary	$888,570	$894,286	$900,076
GM/GS-15	129	131	131
GM/GS-14	284	291	293
GM/GS-13	357	367	369
GS-12	433	439	440
GS-11	494	502	502
GS-10	23	23	23
GS-9	145	148	148
GS-8	123	125	125
GS-7	211	214	214
GS-6	51	52	52
GS-5	27	30	30
GS-4	14	14	14
GS-3	7	7	7
GS-2	11	11	11
GS-1	3	3	3
Subtotal	2,312	2,357	2,362
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	1	1	1
Director Grade	15	15	15
Senior Grade	22	22	22
Full Grade	21	21	21
Senior Assistant Grade	23	24	24
Assistant Grade	7	6	6
Subtotal	89	89	89
Ungraded	665	653	653
Total permanent positions	2,405	2,472	2,477
Total positions, end of year	3,071	3,104	3,109
Total full-time equivalent (FTE) employment, end of year	2,905	2,917	2,917
Average ES salary	$177,714	$178,857	$180,015
Average GM/GS grade	0.0	0.0	0.0
Average GM/GS salary	$92,521	$94,524	$95,781

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

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.

Budget Authority by Activity*
(Dollars in Thousands)

Detail	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget	
	FTE	Amount	FTE	Amount	FTE	Amount
Research Support and Administrative	869	$704,110	878	$711,151	878	$728,930
Office of Research Facilities, Development & Operations	687	499,131	691	504,122	691	516,725
Center for Information Technology	310	360,874	312	364,483	312	373,595
Clinical Center	2	209	2	211	2	216
TOTAL	**1,868**	**$1,564,324**	**1,883**	**$1,579,967**	**1,883**	**$1,619,466**

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

Budget Authority by Object Class*

(Dollars in Thousands)

		FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Total compensable workyears:				
	Full-time employment	1,883	1,883	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$172	$173	$1
	Average GM/GS grade	11.5	11.5	0.0
	Average GM/GS salary	$92	$94	$2
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$82	$83	$0
	Average salary of ungraded positions	$125	$127	$0
	OBJECT CLASSES	**FY 2015 Enacted**	**FY 2016 President's Budget**	**FY 2016 +/- FY 2015**
	Personnel Compensation			
11.1	Full-Time Permanent	$179,447	$183,933	$4,486
11.3	Other Than Full-Time Permanent	9,859	10,056	197
11.5	Other Personnel Compensation	8,414	8,549	135
11.7	Military Personnel	2,330	2,357	28
11.8	Special Personnel Services Payments	670	676	7
11.9	**Subtotal Personnel Compensation**	**$200,719**	**$205,571**	**$4,853**
12.1	Civilian Personnel Benefits	$49,728	$50,424	$696
12.2	Military Personnel Benefits	1,238	1,253	15
13.0	Benefits to Former Personnel	1,712	1,712	0
	Subtotal Pay Costs	**$253,398**	**$258,961**	**$5,564**
21.0	Travel & Transportation of Persons	$506	$511	$5
22.0	Transportation of Things	843	851	8
23.1	Rental Payments to GSA	52,694	53,485	790
23.2	Rental Payments to Others	90,178	91,260	1,082
23.3	Communications, Utilities & Misc. Charges	120,731	121,938	1,207
24.0	Printing & Reproduction	17	17	0
25.1	Consulting Services	$130,794	$134,979	$4,185
25.2	Other Services	281,440	287,069	5,629
25.3	Purchase of goods and services from government accounts	362,791	378,891	16,101
25.4	Operation & Maintenance of Facilities	$74,887	$77,508	$2,621
25.5	R&D Contracts	113	116	3
25.6	Medical Care	551	565	14
25.7	Operation & Maintenance of Equipment	128,536	128,763	227
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$979,112**	**$1,007,891**	**$28,780**
26.0	Supplies & Materials	$49,448	$50,684	$1,236
31.0	Equipment	32,996	33,821	825
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	0	0	0
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	45	47	1
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$1,326,570**	**$1,360,506**	**$33,936**
	Total Budget Authority by Object Class	**$1,579,968**	**$1,619,467**	**$39,499**

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

Detail of Positions*

GRADE	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Total, ES Positions	5	5	5
Total, ES Salary	$857,759	$861,200	$866,200
GM/GS-15	88	85	85
GM/GS-14	249	246	246
GM/GS-13	503	455	455
GS-12	283	296	296
GS-11	100	108	108
GS-10	1	2	2
GS-9	83	87	87
GS-8	33	32	32
GS-7	92	94	94
GS-6	19	20	20
GS-5	11	14	14
GS-4	11	5	5
GS-3	10	9	9
GS-2	12	8	8
GS-1	2	2	2
Subtotal	1,497	1,463	1,463
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	2	2
Full Grade	6	7	7
Senior Assistant Grade	4	5	5
Assistant Grade	1	1	1
Subtotal	21	21	21
Ungraded	368	368	368
Total permanent positions	1,820	1,827	1,827
Total positions, end of year	1,887	1,899	1,899
Total full-time equivalent (FTE) employment, end of year	1,868	1,883	1,883
Average ES salary	$171,552	$172,240	$173,240
Average GM/GS grade	0.0	0.0	0.0
Average GM/GS salary	$91,212	$92,124	$94,427

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

BUDGET MECHANISM TABLE

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

(Dollars in Thousands)

MECHANISM	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	225	$139,096	272	$165,502	278	$178,342	6	$12,840
Administrative Supplements	*(86)*	19,278	*(89)*	20,000	*(64)*	14,367	*(-25)*	-5,633
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	149	161,477	166	171,830	159	161,293	-7	-10,537
Supplements	7	2,633	0	0	0	0	0	0
Subtotal, Competing	156	$164,109	166	$171,830	159	$161,293	-7	-$10,537
Subtotal, RPGs	381	$322,483	438	$357,332	437	$354,002	-1	-$3,330
SBIR/STTR	0	0	0	0	0	0	0	0
Research Project Grants	381	$322,483	438	$357,332	437	$354,002	-1	-$3,330
Research Centers:								
Specialized/Comprehensive	31	$51,892	34	$54,465	32	$47,901	-2	-$6,564
Clinical Research	10	17,407	10	22,656	10	18,484	0	-4,172
Biotechnology	1	3,389	3	2,665	3	2,651	0	-14
Comparative Medicine	3	8,005	3	6,249	0	0	-3	-6,249
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	45	$80,693	50	$86,035	45	$69,036	-5	-$16,999
Other Research:								
Research Careers	16	$2,249	27	$4,240	25	$4,237	-2	-$3
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	58	43,397	55	36,482	105	65,930	50	29,448
Other Research	74	$45,645	82	$40,722	130	$70,167	48	$29,445
Total Research Grants	500	$448,822	570	$484,089	612	$493,205	42	$9,116
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	0	3,834	0	15,497	0	26,381	0	10,884
Total Research Training	0	$3,834	0	$15,497	0	$26,381	0	$10,884
Research & Develop. Contracts	0	$43,728	0	$11,697	0	$11,697	0	$0
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Intramural Research	0	20,624	0	18,155	0	18,155	0	0
Res. Management & Support	0	14,167	0	16,201	0	16,201	0	0
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	0	$531,174	0	$545,639	0	$565,639	0	$20,000

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

MAJOR CHANGES IN THE FISCAL YEAR 2016 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 2016 President's Budget for the Common Fund, which is $20.000 million more than the FY 2015 Enacted level, for a total of $565.639 million.

Research Project Grants (-$3.330 million; total $354.002 million): The Common Fund expects to support a total of 437 Research Project Grant (RPG) awards in FY 2016. Noncompeting RPGs will increase by 6 awards and $12.840 million. New RPGs will be awarded in Common Fund programs to be launched in FY 2016 as well as in new initiatives within ongoing Common Fund programs.

Research Centers (-$16.999 million; total $69.036 million): The Common Fund plans to support a total of 45 Research Center Awards in FY 2016. The decrease in support is due to the completion of the first phase of support for initiatives within the Protein Capture, Illuminating the Druggable Genome, and Knockout Mouse Phenotyping programs. Assessments of these programs will determine whether a second phase of support is warranted.

Other Research (+$29.445 million; total $70.167 million): The estimated increase in Common Fund support for the Other Research mechanism includes a request to use $30 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 2016 is a planned ramping up of the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, a high risk, goal-driven endeavor to develop novel therapies based on neuromodulation of organ function.

Research Training (+$10.884 million; total $26.381 million): The Common Fund plans to support $26.381 million in institutional training awards in FY 2016. The increase in support is due to increases in training activities within the Big Data to Knowledge program, and the inclusion of additional trainees within the Building Infrastructure Leading to Diversity (BUILD) initiative, part of the Enhancing the Diversity of the NIH-Funded Workforce program.

BUDGET BY INITIATIVE

National Institutes of Health
Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
4D Nucleome				
Technology Development, Biological Validation, Modeling and Pilot Mapping	0	10,038	10,038	0
Nucleomic, Imaging, and Computational Tool Development	0	10,068	10,068	0
4D Nucleome Coordination and Integration	0	4,665	7,842	3,177
Subtotal, 4D Nucleome	0	24,771	27,948	3,177
Big Data to Knowledge (BD2K)				
Big Data to Knowledge (BD2K)	8,594	43,466	62,961	19,495
Enhancing the Diversity of the NIH-Funded Workforce				
BUILD Initiative	27,622	44,699	47,524	2,825
National Research Mentoring Network (NRMN)	2,542	1,977	2,158	181
Coordination and Evaluation Center (CEC)	2,326	2,021	1,465	(556)
Subtotal, Enhancing the Diversity of the NIH-Funded Workforce	32,490	48,697	51,147	2,450
Epigenomics				
Mapping Centers	1,102	22	0	(22)
Human Health and Disease	3,511	2,960	0	(2,960)
Technology Development in Epigenetics	4,347	0	0	0
Pharmacology	3,894	4,018	4,000	(18)
Subtotal, Epigenomics	12,854	7,000	4,000	(3,000)
Genotype-Tissue Expression (GTEx) Resources				
Genotype-Tissue Expression (GTEx) Resources	54,280	11,078	4,114	(6,964)
Global Health				
Medical Education Partnership Initiative (MEPI)	3,000	3,000	3,000	0
Human Heredity and Health in Africa (H3Africa)	11,845	9,102	8,443	(659)
Subtotal, Global Health	14,845	12,102	11,443	(659)
Glycoscience				
Accelerating Translation of Glycoscience: Integration and Accessibility	0	9,362	19,862	10,500
High-Risk Research				
NIH Director's Pioneer Award	26,123	22,546	10,877	(11,669)
NIH Director's New Innovator Award Program	106,262	88,648	80,300	(8,348)
Transformative R01's	52,710	50,633	39,432	(11,201)
NIH Director's Early Independence Award Program	18,574	19,244	19,216	(28)
Subtotal, High-Risk Research	203,669	181,071	149,825	(31,246)
Human Microbiome				
Sequence a Reference Set of Genomes	1,968	0	0	0
Evaluation of multi-'omic data in understanding the microbiome's role in health and disease	8,603	6,711	1,833	(4,878)
Subtotal, Human Microbiome	10,571	6,711	1,833	(4,878)
Illuminating the Druggable Genome				
Knowledge Management Network	2,900	3,329	0	(3,329)
Technology Development	2,642	2,659	2,588	(71)
Subtotal, Illuminating the Druggable Genome	5,542	5,988	2,588	(3,400)

National Institutes of Health
Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Knockout Mouse Phenotyping Program				
Production, Characterization, and Cryopreservation	8,467	6,711	0	(6,711)
Phenotyping and Data Release	7,958	6,501	0	(6,501)
Data Coordination	638	526	0	(526)
Subtotal, Knockout Mouse Phenotyping Program	17,063	13,738	0	(13,738)
NIH Center for Regenerative Medicine (NCRM)				
NIH Center for Regenerative Medicine (NCRM)	983	0	0	0
Cell Therapy Projects	1,548	1,250	1,250	0
Cell-Based Screenings	6,791	6,750	6,750	0
Subtotal, NIH Center for Regenerative Medicine (NCRM)	9,322	8,000	8,000	0
Pediatric Research Program				
Gabriella Miller Kids First Research Act	0	12,600	12,600	0
Science of Behavior Change				
Mechanisms of Change	3,766	0	0	0
Science of Behavior Change 2	0	6,730	5,782	(948)
Subtotal, Science of Behavior Change	3,766	6,730	5,782	(948)
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions				
Functional and Anatomical Mapping of Five Organ Systems	0	1,055	18,055	17,000
Next Generation Tools	0	2,179	11,179	9,000
Off-Label Use of Existing Market-Approved Technology for Small Markets	0	205	3,205	3,000
Data Coordination	0	79	1,079	1,000
Subtotal, S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	0	3,518	33,518	30,000
Building Blocks, Biological Pathways and Networks				
National Technology Centers for Networks and Pathways (TCNPs)	110	0	0	0
Extracellular RNA Communication				
Data Management and Resource/Repository (DMRR)	2,492	2,438	2,436	(2)
Reference Profiles of Human Extracellular RNA	4,137	4,578	4,078	(500)
Extracellular RNA Biogenesis, Biodistribution, Uptake, and Effector Function	7,531	7,533	7,177	(356)
Clinical Utility of Extracellular RNAs as Biomarkers and Therapeutic Agents	8,939	14,588	16,132	1,544
Subtotal, Extracellular RNA Communication	23,099	29,137	29,823	686
Gulf Long-term Follow-up of Workers Study				
Gulf Long-term Follow-up of Workers Study	2,500	3,000	0	(3,000)
Health Care Systems Research Collaboratory				
NIH-HMORN Coordinating Center	3,355	2,133	2,116	(17)
Expansion Activities	10,719	10,355	10,642	287
Subtotal, Health Care Systems Research Collaboratory	14,074	12,488	12,758	270
Health Economics				
Changing Incentives for Consumers, Insurers, and Providers	625	554	200	(354)
Science of Structure, Organization, and Practice Design in the Efficient Delivery of Healthcare	3,943	4,419	3,871	(548)
Economics of Prevention	3,787	3,283	2,816	(467)
Data Infrastructure to Enable Research on Health Reform	495	79	431	352
Subtotal, Health Economics	8,850	8,335	7,318	(1,017)
Library of Integrated Network-Based Cellular Signatures (LINCS)				
Perturbation-Induced Data and Signature Generation Centers (U54)	10,199	11,080	10,000	(1,080)

National Institutes of Health
Common Fund by Initiative
(Dollars in Thousands)

(Dollars in Thousands)	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Metabolomics				
Comprehensive Metabolomics Research Cores	12,725	10,969	9,935	(1,034)
Interdisciplinary Training in Metabolomics	5,281	3,553	3,554	1
Metabolomics Technology Development	2,632	2,503	1,888	(615)
Metabolomics Reference Standards Synthesis	1,872	1,926	1,967	41
Metabolomics Data Sharing and Program Coordination Core	1,540	1,913	2,221	308
Subtotal, Metabolomics	24,050	20,864	19,565	(1,299)
Molecular Libraries and Imaging				
Creation of NIH Bioactive Small Molecule Library & Screening Centers	573	0	0	0
Nanomedicine				
Nanomedicine Development Centers	12,000	180	0	(180)
Protein Capture				
Antigen Production	1,932	0	0	0
Production of anti-TF antibodies	3,090	3,453	0	(3,453)
New Reagent Technology Development and Piloting	486	125	0	(125)
Subtotal, Protein Capture	5,508	3,578	0	(3,578)
Re-engineering the Clinical Research Enterprise				
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	298	0	0	0
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and CRTP and MSTP Expansions	1,100	0	0	0
Subtotal, Re-engineering the Clinical Research Enterprise	1,398	0	0	0
Regulatory Science				
Microphysiological Systems for Drug Efficacy and Toxicity Testing	4,931	4,000	4,000	0
Structural Biology				
Membrane Protein Production	9	0	0	0
Single Cell Analysis				
Pilot Studies to Evaluate Cellular Heterogeneity	7,538	6,221	6,003	(218)
Exceptionally Innovative Tools and Technologies for Single Cell Analysis	4,691	4,535	2,939	(1,596)
Accelerating the Integration and Translation of Technologies to Characterize Biological Processes at the Single Cell Level	8,317	7,503	5,398	(2,105)
Single Cell Analysis Challenges	823	95	100	5
Subtotal, Single Cell Analysis	21,369	18,354	14,440	(3,914)
Undiagnosed Disease Program				
Undiagnosed Diseases Program Network	18,690	28,800	29,900	1,100
Training in the Use of Contemporary Genomic Approaches to Rare Disease Diagnostics	935	900	900	0
Subtotal, Undiagnosed Disease Program	19,625	29,700	30,800	1,100
Strengthening the Biomedical Research Workforce				
Director's Workforce Innovation Award to Enhance Biomedical Research Training	6,542	6,750	6,750	0
Strategic Planning Funds	3,341	3,341	3,341	0
Subtotal Common Fund	531,174	545,639	534,416	(11,223)
New Initiatives in Common Fund	0	0	31,223	31,223
Total Common Fund	531,174	545,639	565,639	20,000

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 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 + /- FY 2015
BA	$531,174,000	$545,639,000	$565,639,000	$20,000,000
FTE	0	0	0	0

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

Overview

The NIH Common Fund supports research in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserve special emphasis; that would benefit from strategic coordination and planning across the NIH ICs; and that are designed to address specific, high-impact goals and milestones within a 5 to 10 year timeframe. Collectively, Common Fund programs represent strategic investments aimed at solving problems or building resources to catalyze research throughout the entire biomedical research enterprise. Many Common Fund program support the NIH Director's priority themes for FY 2016:

1. Unraveling Life's Mysteries through Basic Research
2. Translating Discovery into Health
3. Harnessing Data and Technology to Improve Health
4. Preparing a Diverse and Talented Biomedical Research Workforce

Significant efforts are being made to evaluate Common Fund programs during their lifetime and outcomes are assessed as programs end. Funds freed as the programs end or move to other sources of support will be available in FY 2016 for new challenges and opportunities. Strategic planning is therefore a substantial activity as NIH works with stakeholders to identify new NIH-wide priorities for the Common Fund.

Overall Budget Policy: The FY 2016 President's Budget Request for the Common Fund is $565.639 million, an increase of $20.000 million, or 3.7 percent above the FY 2015 Enacted level. The Common Fund will continue to support high priority research with trans-NIH relevance in FY 2016. 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 Descriptions and Accomplishments

The Common Fund supports approximately 30 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. The Common Fund highlights here programs that exemplify the science to be supported in FY 2016 and that involve budget shifts of $3 million or more compared to FY 2015. Also included are Common Fund programs that will be supported in a second phase to address additional scientific challenges and emerging opportunities.

Program Portrait: 4D Nucleome

FY 2015 Level: $ 24.771 million
FY 2016 Level: $ 27.948 million
Change: +$3.177 million

It is estimated that each human cell contains approximately 2 meters (6.5 feet) of linear DNA, squeezed inside the cell's microscopic nucleus. We now know that DNA is not randomly arranged within the nucleus; instead, the organization of the nucleus is tightly controlled and early information suggests that this organization plays a role in cell function. However, specific consequences of this organization are not well understood. The Common Fund's 4D (four dimensional) Nucleome program (http://commonfund.nih.gov/4Dnucleome/index) aims to understand principles underlying nuclear organization in space (three dimensions) and time (the fourth dimension), the role nuclear organization plays in gene expression and cellular function, and how changes in nuclear organization affect normal development as well as various diseases. This program will develop technologies, resources, and data to enable the study of the 4D Nucleome, including novel tools to explore the dynamic nuclear architecture and its role in gene expression programs, models to examine the relationship between nuclear organization and function in both normal development and disease, and reference maps of nuclear architecture in a variety of cells and tissues. In FY 2016, the 4D Nucleome program will expand to include a pool of Opportunity Funds that will be used to support new projects and initiatives addressing identified needs arising throughout the lifetime of the program.

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 ICs, 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 techniques associated with big data usage, and establish a network of collaborating centers of excellence. The expectation is that implementation of BD2K will result in sweeping cultural changes in the way the biomedical research community shares, accesses, queries, cites, and analyzes data.

In FY 2016, it is anticipated that BD2K will be running at full capacity with coordinated efforts underway and the biomedical community engaged with NIH in increasing the accessibility and reuse of biomedical big data and the training of data scientists.

Budget Policy: The FY 2016 President's Budget Request is $62.961 million for the BD2K program from the Common Fund, an increase of $19.495 million or 44.9 percent above the FY 2015 Enacted level. This estimated increase in funding will be used to support activities described above, including increases in the Centers of Excellence for Biomedical Big Data and enhanced efforts in training and data coordination.

Enhancing the Diversity of the NIH-Funded Workforce

NIH has long recognized that diversity in the biomedical and behavioral research workforce is critical to ensuring that the brightest and most creative minds are contributing to scientific and technological advancements. However, demographic data demonstrating persistent underrepresentation of certain groups and recent research findings have suggested that additional investments using different approaches are needed. In particular, the powerful impact that psychosocial factors play in encouraging or deterring the pursuit of science careers, especially among groups traditionally underrepresented in science fields, and has been demonstrated. Importantly, effectiveness of interventions targeting psychosocial factors in promoting persistence in the sciences has also been demonstrated. The Enhancing the Diversity of the NIH-Funded Workforce program (http://commonfund.nih.gov/diversity) aims to scale these recent approaches and integrate them with rigourous biomedical research training to develop and test unique innovative interventions to transform the culture and effectiveness of research training and mentoring.

This program consists of three highly integrated initiatives. The Building Infrastructure Leading to Diversity (BUILD) initiative is a set of experimental training awards designed to implement and assess interventions at the institutional, social, and individual levels aiming to attract students from diverse backgrounds into the training pipeline and to encourage their persistence to become future NIH-supported researchers. The National Research Mentoring Network (NRMN) is developing novel mentoring strategies, establishing standards and training for mentors, and developing a diverse network of mentors and mentees across the country. The Coordination and Evaluation Center (CEC) is working across all initiatives and awardee institutions to examine which interventions are most effective and within what contexts, and is responsible for disseminating lessons learned to the broad biomedical research training community, thus ultimately strengthening the entire biomedical research enterprise.

In FY 2016, the BUILD initiative budget will expand to incorporate additional trainees within existing awards.

Budget Policy: The FY 2016 President's Budget Request is $51.147 million for the Enhancing the Diversity of the NIH-Funded Workforce program from the Common Fund, an increase of $2.450 million, or 5.0 percent above the FY 2015 Enacted level. The estimated increase in funding will be used to support additional trainees within the BUILD initiative.

Epigenomics
Epigenomics is the field of biomedical research focused on DNA modifications and modifications of proteins associated with DNA. These modifications, collectively called the "epigenome," occur "on top of" the linear DNA that makes up the genome and can be associated with changes in gene activity without altering the underlying DNA sequence. 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 in human health and disease. The Epigenomics program has generated 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 also published landmark studies on the role of epigenomic modifications in normal development and disease and are developing novel approaches to analyze the data in the context of different diseases.

In FY 2016, the Epigenomics program undergoes a planned decrease as awards to undertake computational analyses using the publicly available epigenomic reference maps are completed.

Budget Policy: The FY 2016 President's Budget Request is $4.000 million for the Epigenomics program, a decrease of $3.000 million, or 42.9 percent below the FY 2015 Enacted level. This decrease reflects the planned completion of the Computational Analyses Exploiting Reference Epigenomic Maps activity within the Human Health and Disease initiative.

Genotype-Tissue Expression
Some diseases result from sequence variation within the protein-coding region of specific genes; however, many diseases involve changes in DNA sequences that lie outside of any protein-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, uncovering valuable insights into the mechanisms of gene regulation and how perturbations in gene expression may be related to various diseases. 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. Data from the GTEx program will strengthen the power of genome-wide association studies to identify potential new gene targets for therapies.

In FY 2016, the GTEx program will undergo a planned decrease as the primary deliverables of the program, including biospecimens, gene variation and expression data, and statistical methods, will be in place.

Budget Policy: The FY 2016 President's Budget Request is $4.114 million for the GTEx program, a decrease of $6.964 million, or 62.9 percent below the FY 2015 Enacted level. The estimated decrease reflects the planned decrease in initiatives for a Laboratory, Data Analysis, and Coordinating Center, statistical methods, and molecular analyses of biospecimens.

Global Health

NIH has a longstanding commitment to address both infectious and noninfectious diseases around the world, including in low- and middle-income nations that face a persistent cluster of infectious disease, malnutrition, and a growing incidence of chronic diseases and disabilities. Strategic investment by the Common Fund's Global Health program (http://commonfund.nih.gov/globalhealth/index) is intended to build capacity for research in Africa, since research in Africa is vital not only for health of Africans but for the understanding of human genetic diversity and the impact this has on health and disease everywhere. This program fosters teamwork among scientists and health organizations, builds infrastructure, and increases capacity to improve medical training and retention of trained personnel to understand and treat disease more aggressively. The Global Health program consists of two initiatives. The Medical Education Partnerships Initiative (MEPI), in partnership with the President's Emergency Plan for AIDS Relief (PEPFAR), is strengthening medical education systems in Africa and creating an environment that values and nurtures research as part of a strategy to increase the number and retention of quality health care professionals. The Human Heredity and Health in Africa (H3Africa) initiative, a partnership between NIH and the Wellcome Trust, supports the development of expertise among African scientists in the study of genomics and environmental factors of common diseases by investing in research, training, and infrastructure, and the establishment of networks of African investigators.

In FY 2016, the Global Health program will support a second phase of MEPI focused on research and career training support for junior faculty and institutional research support capacity.

Budget Policy: The FY 2016 President's Budget Request is $11.443 million for the Global Health program, a decrease of $0.659 million, or 5.4 percent below the FY 2015 Enacted level. This level of funding reflects a planned decrease in support for the H3Africa biorepository, and includes support for a second phase of MEPI as described above.

Program Portrait: Glycoscience

FY 2015 Level: $9.362 million
FY 2016 Level: $19.862 million
Change: +$10.500 million

Glycoscience is the study of how the addition of sugar modifications to proteins change the way the proteins function in important ways. All cells carry an array of sugars, or glycans, that have the ability to modulate or mediate cellular interactions with other cells, the surrounding cellular matrix, and molecules critical to development and function of complex multicellular organisms. Certain types of glycans play important roles in mediating additional cellular processes, including growth of neurons and communication between neuronal synapses. However, the complexity of carbohydrate chemistry makes the analysis of glycans inaccessible to most biomedical researchers. The Common Fund's Glycoscience program (http://commonfund.nih.gov/Glycoscience/index) will develop methodologies and resources to make the study of glycans more accessible to the broad biomedical research community. This program aims to develop methods and technologies to synthesize glycans, tools for probing and analyzing glycans and their interacting partners, and tools for data analysis and integration. The Glycoscience program will expand in FY 2016 to develop additional tools, technologies, and methods for synthesis, identification, manipulation, and analysis for a range of biomedically relevant glycans.

High-Risk High-Reward Research

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 Common Fund's High-Risk High-Reward program (http://commonfund.nih.gov/highrisk/index.aspx) includes four complementary initiatives that support exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH mission. These initiatives include the Pioneer Awards, New Innovator Awards, Transformative Research Awards, and Early Independence Awards. Since the High-Risk High-Reward program tests new ways of supporting innovation, NIH commissioned a rigorous external evaluation of the most mature of these initiatives, the Pioneer Awards. Comparison of research from Pioneer Awards, R01s (NIH's most common project-based grant mechanism), 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, NIH ICs have embraced these funding mechanisms and have committed to their support. In addition to supporting awardees within the Common Fund's High-Risk High-Reward program, several ICs now are implementing similar programs of their own.

As noted above, Common Fund programs are designed to be short-term, thus in FY 2016, Common Fund support for the High-Risk High-Reward program decreases slightly, as ICs increase support for Pioneer, New Innovator, and Transformative Research Awards future year costs. Beginning in FY 2014, the Pioneer and Transformative Research Awards have been supported by the Common Fund during the first year, while ICs provide future years of support. Thus, the Common Fund budget of this program appears to steadily decrease over the years as the Common Fund pays less of the future year costs of each award. Additionally, ICs support the full amounts of some New Innovator Awards. IC support of the High-Risk High-Reward awards is based on the IC's enthusiasm for innovative research conducted through these awards within their IC mission. Although it is not possible to determine the exact amount of IC support in FY 2016, it is anticipated to increase based on the ICs steady increase in support over prior years.

Budget Policy: The FY 2015 President's Budget Request is $149.825 million for the High-Risk High-Reward program, a decrease of $31.246 million, or 17.2 percent below the FY 2015 Enacted level. This decrease reflects the planned increase in IC support for Pioneer, New Innovator, and Transformative Research Awards.

Human Microbiome Project

Our bodies are inhabited by trillions of microorganisms living together with our human cells. While many of these bacteria, viruses, and fungi are beneficial, others are implicated in diseases such as asthma, cancer, and obesity. In FY 2008, the Common Fund launched the Human Microbiome Project (HMP) (http://commonfund.nih.gov/hmp/index) to create a national resource of microbial sequence data, analysis tools, and methods; enable studies to identify and characterize hundreds of new human microbes; and explore causal links between changes in the microbiome and disease. HMP has achieved many notable successes, including the analysis of microbiomes from over 300 healthy individuals, leading to the insight that there is surprising

variability in microbiomes between individuals and paving the way for numerous studies that are beginning to examine how changes in the microbiome correlate with disease. More recent efforts focused on creating the first integrated dataset of microbial and host properties from cohort studies of microbiome-associated diseases. Catalyzed in part by the foundational resources and data sets generated by HMP, many NIH ICs are now investigating the human microbiome within the context of their individual research missions, and support for microbiome research across NIH has greatly increased.

HMP will undergo a planned decrease in FY 2016, as the final Common Fund initiative to gather data on proteins and metabolites produced by the microbiome winds down. Work on the microbiome is increasingly being supported by a number of NIH Institutes and Centers, in part due to the catalytic data and resources developed by HMP.

Budget Policy: The FY 2016 President's Budget Request is $1.833 million for the Human Microbiome Project, a decrease of $4.878 million, or 72.7 percent below the FY 2015 Enacted level. This decrease reflects the planned completion of the final initiative to evaluate multi-omic data (proteomic, metabolomic, etc.) to understand the microbiome's role in health and disease.

Illuminating the Druggable Genome

The overarching goal of the Common Fund's Illuminating the Druggable Genome (IDG) (http://commonfund.nih.gov/idg/index) program is to improve knowledge of the properties and functions of understudied proteins that are related to known drug targets, and are thus likely candidates to be drug targets themselves. This program focuses on hundreds of understudied proteins within four protein families that are commonly targeted for drug development –G-protein-coupled receptors, nuclear receptors, ion channels, and protein kinases. Designed as a two phase program, the current pilot phase aims to create a data resource that will catalog known information about these protein families and establish strategies for obtaining further information about the function of these proteins so that investigators can determine whether a given protein is a likely target for a disease or condition of interest. Ultimately, this program will catalyze discovery of truly novel biology and provide a wealth of new candidates for therapeutic development. Launched in FY 2014, the IDG pilot phase will undergo a review of the outcomes in FY 2015. If merited, Common Fund support of IDG would expand in FY 2016 to support the second phase of data coordination and high throughput approaches to analyze protein function.

Budget Policy: The FY 2016 President's Budget Request is $2.588 million for the Illuminating the Druggable Genome program, a decrease of $3.400 million, or 56.8 percent below the FY 2015 Enacted level. This decrease reflects the planned wind down of the pilot phase. However, if the program review reveals additional scientific challenges and opportunities in this area, the program will expand in FY 2016 to accommodate a second phase.

Knockout Mouse Phenotyping Program

Recognizing the value and utility of a readily-accessible, genome-wide collection of mouse mutants for determining how mammalian genes function, several international programs were launched to develop mutant mouse strains. Collectively, these programs have generated more than 8,000 prototype knockout mice. The Common Fund has joined together with multiple

NIH ICs to support the Knockout Mouse Phenotyping Program (KOMP2), which builds upon this existing resource by expanding the efforts to characterize the mutant strains, including mutations that result in embryonic lethality. The data are being made rapidly available to the entire research community through an internationally coordinated data coordinating center as a way to catalyze additional analyses of how specific genes contribute to health and disease conditions. Some of the genes to be characterized are expected to suggest novel drug targets and increase understanding of genetic pathways that drugs may affect. In FY 2016, the Common Fund may support a second phase of KOMP2 to enable enhanced phenotyping efforts incorporating new technology and using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) techniques to mutate the genome more efficiently.

Budget Policy: The FY 2016 President's Budget Request is $ 0.000 million for the KOMP2 program, a decrease of $13.738 million, or 100.0 percent below the FY 2015 Enacted level. This decrease reflects the planned completion of the first phase of the program. However, if the program review reveals additional scientific challenges and opportunities in this area, the program will expand in FY 2016 to accommodate a second phase.

NIH Center for Regenerative Medicine

The NIH Center for Regenerative Medicine (NIH CRM) (http://commonfund.nih.gov/stemcells/index) aims to work through scientific and regulatory hurdles to the development of induced pluripotent stem cells (iPSCs) for clinical use. iPSCs are generated by coaxing adult cells into reverting back to an embryonic stem cell-like state, which then can generate many different cell types for use in screening or developing therapies. In the first phase of this program, NIH CRM supported pilot projects to develop the potential for using iPSCs to treat several diseases and conditions, developed stem cell lines, drafted standard consent forms, and compiled protocols and procedures used to derive, culture, and differentiate stem cells into different cell types. In the second phase, NIH CRM will support a Therapeutic Challenge award to advance efforts to develop iPSCs as therapy for age-related macular degeneration, a leading cause of blindness in the elderly. The project also will navigate through methodological and regulatory challenges that may be relevant to the broader iPSC research community. Additionally, NIH CRM will support a new facility at the National Center for Advancing Translational Science (NCATS) with three major goals: 1) establish detailed quality control standards to define differentiated (specialized) cell types and pluripotency; 2) develop methods to assess heterogeneity in cultured cells derived from iPSCs; and 3) develop standardized methods to produce mature cells meeting the quality control standards above.

Budget Policy: The FY 2016 President's Budget Request is $8.000 million for NIH CRM, no change from the FY 2015 Enacted level. The estimated funding level reflects ongoing support for the Therapeutic Challenge award and Stem Cell Technology Facility at NCATS.

Pediatric Research Program

In 2014, the Gabriella Miller Kids First Research Act was passed into law, authorizing support for pediatric research within the Common Fund. Funds were appropriated to the Common Fund from the Pediatric Research Initiative Fund in FY 2015 for this purpose. Planning activities are currently under way to identify where strategic investment by the Common Fund can have the largest impact in pediatric research. Beginning in FY 2015, the Common Fund will support

initiatives in pediatric research consistent with the Common Fund mandate to support research in areas of emerging scientific opportunities, rising public health challenges, and knowledge gaps that deserve special emphasis; would benefit from strategic coordination and planning across the NIH ICs; and that are designed to address specific goals and milestones.

After passage of the Act, the Department of the Treasury transferred $38 million to the Pediatric Research Intiative Fund, of which $12.6 million has been appropriated. Under current law, Treasury estimates that it will be able to transfer an additional $42 million in FY 2019 and $45 million in FY 2023 (in other words, one year before each Presidential election).

Budget Policy: The FY 2016 President's Budget Request is $12.600 million for Pediatric Research, no change from the FY 2015 level. These funds will continue to support pediatric research of trans-NIH relevance, with specific activities currently under development.

Science of Behavior Change

Unhealthy human behaviors, such as smoking, drug and alcohol abuse, over-eating, and a failure to exercise, all contribute to negative health outcomes and common diseases. However, it is extremely difficult not only to implement healthy behavior changes, but also to maintain these positive changes over an extended period of time. Uncovering the basic foundations of how motivation changes across a broad array of health-related behaviors can lead to more effective and efficient approaches to behavioral interventions, with the ultimate goal of improving the Nation's health. The first phase of the Common Fund's Science of Behavior Change (SOBC) (http://commonfund.nih.gov/behaviorchange/index) aimed to improve understanding of the basic mechanisms of human behavior change across a broad range of health-related behaviors and use this knowledge to develop more effective behavioral interventions. Research funded by the SOBC program has led to the identification of three broad classes of intervention targets that are highly relevant to understanding the mechanisms of behavior change: self-regulation, stress reactivity and resilience, and interpersonal and social processes.

Beginning in FY 2015, the second phase of the SOBC program will develop measures and techniques that afford a more mechanistic, experimental medicine approach to behavior change, where interventions are designed to engage the putative targets identified in phase one and engagement of those targets is routinely assessed via reliable and validated assays. The program will also include an important new focus on adherence to medical regimens and other high priority health behaviors that could benefit from this target engagement approach.

Budget Policy: The FY 2016 President's Budget Request is $ 5.782 million for the Science of Behavior Change program, a decrease of $0.948 million, or 14.1 percent below the FY 2015 Enacted level. This funding will allow continued support for initiatives to develop targets for behavior change.

Program Portrait: Stimulating Peripheral Activity to Relieve Conditions (SPARC)

FY 2015 Level: $3.518 million
FY 2016 Level: $33.518 million
Change: +$30.000 million

Modulation of peripheral nerve signals to control organ function has been recognized as a potentially powerful way to treat many diseases and conditions, such as hypertension, heart failure, gastrointestinal disorders, type II diabetes, inflammatory disorders, and more. However, the mechanisms of action for neuromodulation therapies are poorly understood, and consequently efficacy is minimal and side effects are frequent. The Common Fund's Stimulating Peripheral Activity to Relieve Conditions (SPARC) program (http://commonfund.nih.gov/sparc/index) is a high-risk, goal-driven endeavor to develop foundational knowledge and technologies for an entirely new class of neural control devices that have the potential to precisely treat a wide variety of diseases and conditions. The SPARC program will support interdisciplinary teams of investigators to deliver neural circuit maps of several organ systems, novel electrode designs, minimally invasive surgical procedures, and stimulation protocols, driven by an end goal to develop new neuromodulation therapies. The program is expected to be iterative and dynamic, with the novel technologies informing mapping efforts, and mapping results defining new technology requirements. This program will use Other Transaction Authority (OTA) for selected initiatives, which will allow the high levels of flexibility, responsiveness to adjust program components, and ability to engage with non-traditional partners as needed to address specific, high-risk goals within this complex, interdisciplinary, and rapidly evolving area of science. In FY 2016, SPARC will ramp up activities to develop neural circuit maps and generate next generation tools to stimulate peripheral nerves. Additionally, SPARC will launch new FY 2016 activities to explore the utility of existing neuromodulation devices to address new indications and develop a coordinated data resource.

Strategic Planning and Evaluation

The Common Fund's 10 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 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 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 also is 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. The utility of data, resources, technologies, and other program outputs is assessed through surveys and the analysis of bibliometric data such as citation analyses.

Budget Policy: The FY 2016 President's Budget Request is $3.341 million, no change from the the FY 2015 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 and to fund the operating cost for OSC to manage the Common Fund.

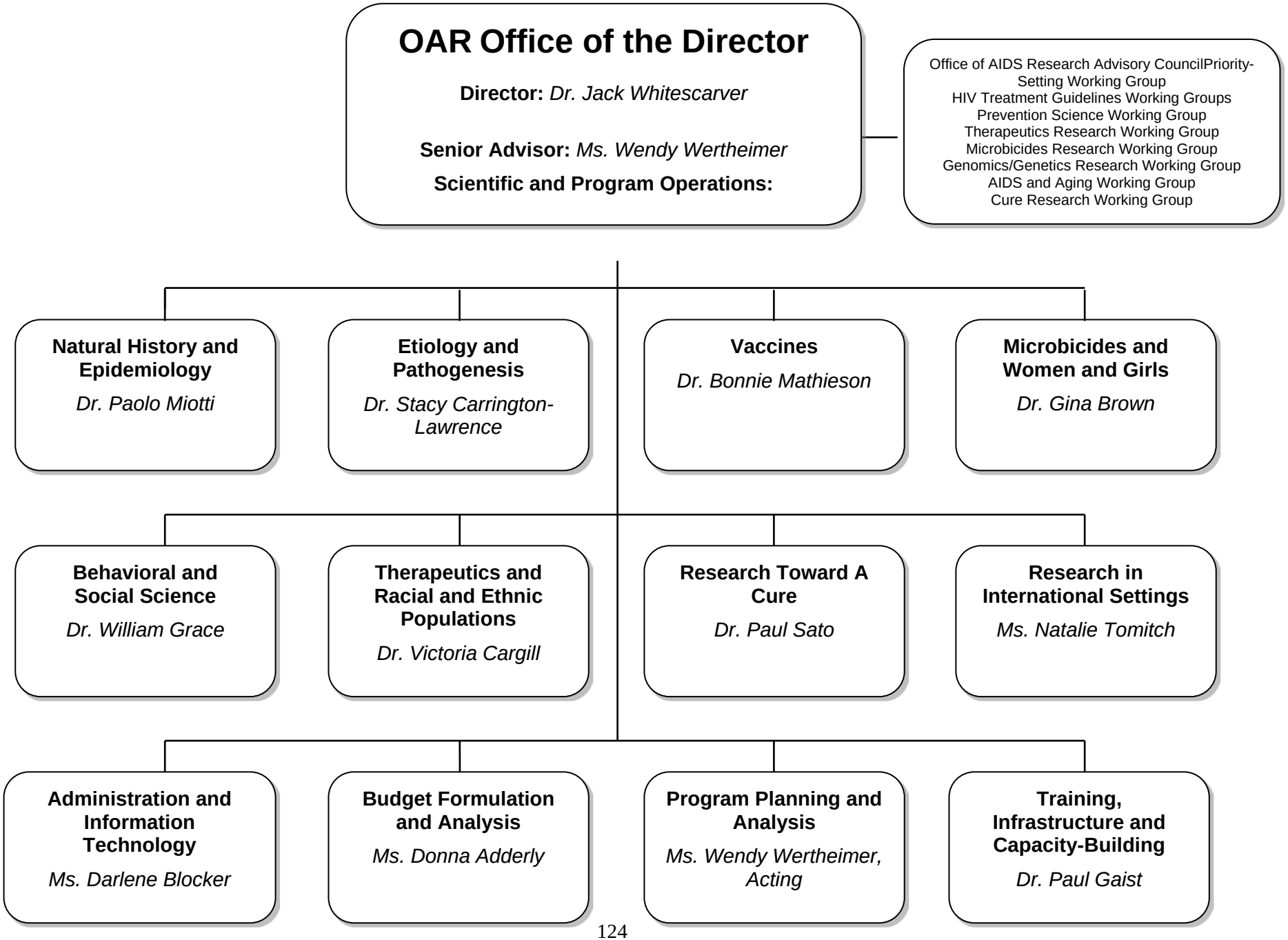
Funds Available for New Programs

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. A potential new Common Fund program for FY 2016 is Enabling Exploration of the Eukaryotic Epitranscriptome (E4). Although great strides have been made in understanding how chemical modifications to DNA or DNA-associated proteins can influence biological processes, much less is known about the effects of modifications to RNA. The E4 program aims to develop tools, technologies, and datasets to enable the systematic study of RNA modifications, collectively called the epitranscriptome. Ultimately, this program will provide fundamental knowledge about RNA modifications and their roles in human health and disease. Another potential new Common Fund program for FY 2016 is Mechanisms of Benefit of Physical Activity. If implemented, this program would deliver data from humans undergoing a variety of physical activity regimens. Investigators interested in many different health conditions will be able to mine this data to explore molecular and cellular mechanisms through which physical activity provides benefit. Additionally, two Common Fund programs (IDG and KOMP2) may be supported for a second phase. Plans for these activities may change in nature or scope depending on scientific opportunities and/or available funding.

Budget Policy: The FY 2016 President's Budget Request is $31.223 million to support new programs and initiatives within the Common Fund. Potential new initiatives will be selected through strategic planning activities designed to identify and understand dongaoing work in each scientific area and to determine what opportunities exist for the Common Fund to have a significant impact.

OFFICE OF AIDS RESEARCH

Trans-NIH AIDS Research Budget


OAR Office of the Director
Director: Dr. Jack Whitescarver
Senior Advisor: Ms. Wendy Wertheimer
Scientific and Program Operations:
Office of AIDS Research Advisory CouncilPriority-Setting Working Group
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. Wendy Wertheimer, Acting
Training, Infrastructure and Capacity-Building
Dr. Paul Gaist

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

Institute / Center	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
NCI	$269,212	$269,660	$281,130	$11,470
NHLBI	64,044	64,974	66,552	1,578
NIDCR	18,414	17,465	18,002	537
NIDDK	29,952	30,031	31,262	1,231
NINDS	45,345	45,465	45,619	154
NIAID	1,563,878	1,586,804	1,648,753	61,949
NIGMS	64,096	64,963	67,147	2,184
NICHD	140,245	142,016	147,069	5,053
NEI	1,740	1,360	925	-435
NIEHS	5,165	5,179	5,179	--
NIA	5,451	5,465	5,700	235
NIAMS	4,766	4,779	4,999	220
NIDCD	1,816	1,821	1,847	26
NIMH	157,005	156,687	163,521	6,834
NIDA	300,714	298,862	302,211	3,349
NIAAA	27,464	27,537	29,189	1,652
NINR	12,234	12,266	12,757	491
NHGRI	6,900	6,380	6,411	31
NIBIB	1,220	713	395	-318
NIMHD	19,787	21,839	23,367	1,528
NCCIH	1,558	975	777	-198
NCATS	66,122	64,287	64,827	540
FIC	23,458	23,520	24,909	1,389
NLM	7,917	7,937	8,437	500
OD				
OAR	61,923	61,923	61,923	--
ORIP	77,153	77,153	77,153	--
Subtotal, OD	139,076	139,076	139,076	--
TOTAL, NIH	**$2,977,579**	**$3,000,061**	**$3,100,061**	**$100,000**

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS [1]

(Dollars in Thousands)

MECHANISM	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,567	$932,970	1,654	$1,289,448	1,637	$1,287,895	-17	-$1,553
Administrative Supplements	*(130)*	29,359	*(61)*	21,726	*(60)*	21,686	*(-1)*	-40
Competing	703	628,085	662	338,415	779	416,298	117	77,883
Subtotal, RPGs	2,270	$1,590,414	2,316	$1,649,589	2,416	$1,725,879	100	$76,290
SBIR/STTR	67	35,217	64	36,256	65	36,015	1	-241
Research Project Grants	2,337	$1,625,631	2,380	$1,685,845	2,481	$1,761,894	101	$76,049
Research Centers:								
Specialized/Comprehensive	61	$142,705	58	$141,708	57	$133,691	-1	-$8,017
Clinical Research	1	61,746	1	59,911	1	60,451	--	540
Biotechnology	0	491	0	246	0	246	--	--
Comparative Medicine	26	58,764	27	59,266	26	58,566	-1	-700
Research Centers in Minority Institutions	13	9,018	9	6,350	7	5,320	-2	-1,030
Research Centers	101	$272,724	95	$267,481	91	$258,274	-4	-$9,207
Other Research:								
Research Careers	236	$40,029	236	$38,614	240	$39,403	4	$789
Cancer Education	0	0	0	0	0	0	--	--
Cooperative Clinical Research	8	14,023	8	14,022	8	14,022	--	--
Biomedical Research Support	0	1,884	0	1,644	0	1,644	--	--
Minority Biomedical Research Support	1	337	1	336	1	336	--	--
Other	157	61,124	159	61,092	163	61,529	4	437
Other Research	402	$117,397	404	$115,708	412	$116,934	8	$1,226
Total Research Grants	2,840	$2,015,752	2,879	$2,069,034	2,984	$2,137,102	105	$68,068
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	98	$4,637	99	$4,309	97	$4,319	-2	$10
Institutional Awards	652	33,404	658	34,023	654	34,095	-4	72
Total Research Training	750	$38,041	757	$38,332	751	$38,414	-6	$82
Research & Develop. Contracts	100	$410,255	102	$382,076	102	$402,428	0	$20,352
(SBIR/STTR) (non-add)	*(2)*	*(537)*	*(4)*	*(1,287)*	*(4)*	*(1,200)*	*0*	*(-87)*
Intramural Research		$336,128		$332,166		$341,625		$9,459
Res. Management and Support		115,480		116,530		118,569		2,039
Res. Management & Support (SBIR Admin) (non-add)								
Office of the Director - Appropriation		*139,076*		*139,076*		*139,076*		--
Office of the Director - Other [2]		61,923		61,923		61,923		--
ORIP (non-add) [2]		*77,153*		*77,153*		*77,153*		--
Total, NIH Discretionary B.A.		**$2,977,579**		**$3,000,061**		**$3,100,061**		**$100,000**

[1] All items in italics and brackets are non-add entries. FY 2014 and FY 2015 levels are shown on a comparable basis to FY 2016.

[2] Number of grants and dollars for the ORIP components of OD are distributed by mechanism and are noted here as a non-add.

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

Area of Emphasis	FY 2012 Actual	FY 2013 Actual	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Vaccines	$556,613	$518,170	$532,671	$537,402	$567,947	$30,545
HIV Microbicides	129,919	111,240	107,843	108,349	113,072	4,723
Behavioral and Social Science	420,084	397,377	411,723	414,873	423,038	8,165
Etiology and Pathogenesis	668,244	625,027	666,569	670,527	698,310	27,783
Therapeutics						
Therapeutics as Prevention	*56,561*	*69,375*	*75,638*	*73,696*	*74,472*	*776*
Drug Discovery, Development, and Treatment	*650,059*	*632,123*	*660,194*	*671,857*	*685,653*	*13,796*
Total, Therapeutics	706,620	701,498	735,832	745,553	760,125	14,572
Natural History and Epidemiology	257,973	243,454	228,830	230,437	236,868	6,431
Training, Infrastructure, and Capacity Building	280,775	261,921	259,866	257,591	264,978	7,387
Information Dissemination	54,567	39,178	34,245	35,329	35,723	394
Total	$3,074,795	$2,897,865	$2,977,579	$3,000,061	$3,100,061	$100,000

The Global AIDS Epidemic

UNAIDS reports that in 2013:

- more than **35 million** people were estimated to be living with HIV/AIDS; the majority do not have access to HIV prevention, care, and treatment; and approximately half are unaware they are infected.
- there were about **2.1 million** new infections or about **6,000 new infections per day**;
- **1.5 million** people died of AIDS-related illnesses. Deaths have declined due in part to scale-up of antiretroviral (ARV) therapy, but HIV remains a leading cause of death worldwide and the number one cause of death in Africa.
- HIV has led to a resurgence of tuberculosis (TB), particularly in Africa, and TB is a leading cause of death for people with HIV worldwide.
- women represented half (50%) of all adults living with HIV worldwide. HIV is the leading cause of death among women of reproductive age.
- 33% of new infections were among young people, ages 15-24
- **3.2 million** children were living with HIV; there were 240,000 new infections among children, and 190,000 AIDS deaths.
- global mother-to-child transmission rates in the absence of antiretroviral drug administration to the mother and infant are 15-30%, and increase to 45% with breastfeeding; 33% of pregnant women in low and middle-income countries do not receive ARV therapy to prevent mother-to child HIV transmission

The AIDS Epidemic in the United States

The Centers for Disease Control (CDC) reports that in the U.S.:

- more than **1.2 million** people are living with HIV
- over **650,000** people have died
- new infections have remained at about **50,000** per year for more than a decade
- while many people with HIV are diagnosed (86%), fewer are engaged in care (40%) and are prescribed ARV treatment (37%)
- only **30%** of individuals living with HIV are virally suppressed (the point at which the virus is under control and a person can remain healthy and reduce the risk of transmission) and viral suppression is even lower among African Americans (21%) and young people ages 25-34 (15%)
- therefore, **70% do not have their virus under control.**

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 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016+/- FY 2015
	$2,977,579,000	$3,000,061,000	$3,100,061,000	$100,000,000

Director's Overview

Groundbreaking Accomplishments but Monumental Challenges: The human and economic toll of the AIDS pandemic is profound. It requires a unique response that is complex, comprehensive, multi-disciplinary, and global. In the three decades since the first cases of AIDS were reported, NIH has been the global leader in research to understand, prevent, diagnose, and treat HIV and its many related conditions. NIH has established a comprehensive and coordinated AIDS research program that has demonstrated unprecedented progress against this worldwide epidemic. 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 vaccine and a cure – are developed and available around the world. Although much has been accomplished, the investment in HIV-related research is just beginning to reap rewards, opening new possibilities and scientific opportunities to make progress against AIDS and its associated illnesses and consequences.

Coordinated Trans-NIH AIDS Research Program: 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). It is essential to point out that because AIDS affects virtually every organ system, with a myriad of HIV-associated infections, malignancies, co-morbidities and clinical complications, NIH AIDS research supports a vast portfolio that also includes research on these related illnesses and conditions, such as tuberculosis; Hepatitis; and AIDS-associated cancers, neurologic complications, and cardiovascular conditions. OAR coordinates the scientific, budgetary, and policy elements of this diverse trans-NIH research program. OAR has established comprehensive trans-NIH planning, budgeting, and portfolio analysis processes to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively. OAR also identifies specific funding for emerging scientific opportunities and public health challenges that require focused attention; manages and

facilitates multi-Institute and trans-Institute activities to address those needs; fosters research by designating funds and supplements to jump-start or pilot program areas; facilitates international AIDS research and training; and sponsors scientific agenda setting workshops to identify new cutting-edge initiatives.

Annual Trans-NIH Strategic Plan and Budget: OAR plans and coordinates this research through the development of an annual Trans-NIH plan that identifies overarching AIDS-research priorities and specific research objectives and strategies. This comprehensive and unique annual process involves scientists from across NIH and other Federal agencies, non-government experts, and constituency groups. OAR also is mandated to develop an annual trans-NIH AIDS research budget explicitly tied to the objectives of the Strategic Plan. Thus, this budget request is informed by the FY 2016 Trans-NIH Plan for HIV-Related Research (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 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.

Priority-Setting Review: The OAR Advisory Council has also reaffirmed the key scientific priorities. Over the past year, OAR conducted a priority-setting portfolio review of the entire AIDS research program to re-examine and affirm the highest priorities for NIH AIDS research. OAR will continue to allocate and redirect resources across the ICs and across the key areas of science to address these priorities.

Challenges and Opportunities for FY 2016: The key scientific priorities for NIH AIDS research that shape the Trans-NIH AIDS research budget request are:

Translating Discovery into Health

- **Prevention Research**: NIH will support research to prevent transmission and acquisition of HIV infection, including basic research on HIV that will underpin further development of critically needed vaccines, microbicides, and other biomedical prevention strategies, including the use of antiretroviral therapy as prevention.
- **Treatment:** NIH will support HIV treatment research to develop and assess therapies that are more effective in suppressing viral replication; less toxic; longer acting; have fewer side effects and complications, such as premature aging co-morbidities; and more likely to achieve eradication of infection. NIH will also address unique characteristics, such as gender, race/ethnicity, age, nutritional status, genetics, and history of violence and trauma that may influence treatment success or failure.
- **Research Toward a Cure:** NIH will support research related to the potential for a cure or lifelong remission of HIV infection, including studies on viral persistence, latency, reactivation, and eradication.
- **Co-Infections, Co-Morbidities and Complications:** NIH will support research on the treatment and prevention of HIV- related co-infections, malignancies, and neurological, cardiovascular, and metabolic complications.
- **Behavioral and Social Science Research:** NIH will support research on understanding factors that fuel or mitigate HIV epidemics; the role of stigma; and adherence to treatment or prevention strategies, particularly to address the HIV Care Continuum.

***Preparing a Diverse and Talented Biomedical Research Workforce*:** NIH will train the next generation of AIDS researchers around the world to foster collaboration, innovation, and transformative research.

Overall Budget Policy:

To address these critical AIDS research priorities, the FY 2016 President's Budget estimate for the trans-NIH AIDS research program is $3,100.061 million, an increase of $100.000 million or 3.3 percent above the FY 2015 Enacted level. The OAR is authorized to allocate all dollars associated with this area of research across the NIH. Therefore, the total for AIDS research includes both extramural and intramural research (including research management support, management fund, and service and supply fund); buildings and facilities; and training and evaluation. The total also includes basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the many HIV-associated malignancies, co-infections, co-morbidities, and complications, including TB, hepatitis C, and HIV-associated cancers. Thus, the total for AIDS-related research is not comparable to spending reported for other individual diseases. This request reflects the shifting of funds across ICs to address new and exciting scientific opportunities in AIDS research identified through OAR's unique trans-NIH strategic planning, priority-setting, portfolio analysis, and budget processes and to address the evolving clinical profile of the epidemic. This request provides increased funding to support high priority basic research (etiology and pathogenesis), the underlying foundation for all HIV prevention and treatment research, as well as research to better understand disease progression and HIV-related co-morbidities. Increased funds are provided for the key priority of prevention research, particularly new opportunities in the development of vaccines. In FY 2015, OAR launched a three-year (FY 2015-2017) commitment to provide $100 million in redirected funds to research towards a cure. OAR provided the initial investment of $15 million in additional cure research in FY 2015, bringing the total to $127.3 million. This FY 2016 request includes a $21.8 million increase to support the second year of the commitment, which will total $149.1 million in FY 2016 (see page 13 for details) . These increased funds are provided for basic research, treatment research, and novel therapeutic vaccine research. Increased funds are also provided for research on new, long-acting, more effective and less toxic ARV therapies for both treatment and prevention.

Program Descriptions and Accomplishments

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 United States 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 2016 President's Budget request for Vaccine research is $567.947 million, an increase of $30.545 million or 5.7 percent above the FY 2015 Enacted level. Innovative basic HIV vaccine research studies will be supported to inform the development of new vaccine concepts that might induce higher levels of protective antibodies and prevent HIV infection more efficiently than vaccines already tested. In FY 2016, 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 candidates 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. Increased support will be provided for clinical trials that evaluate the ability of monoclonal antibodies from HIV-infected individuals. These trials have been initiated in participants in the U.S. and will enable us to understand how they will be able to prevent HIV infection, delay disease progression or eliminate HIV-infected cells. The increases provided to vaccine research reflect OAR's redirections of funds from other scientific areas to support critical research opportunities in this area.

HIV Microbicides: A safe and effective microbicide will be an important asset to the HIV prevention tool kit. Microbicides are products, including antiretroviral (ARV) drugs and other agents, that 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, formulation, 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 ARV-based microbicides as HIV prevention strategies. Studies are underway and being developed to test: different ARV- and non-ARV-based products; the safety of various microbicide formulations, including long acting formulations; the safety and pharmacokinetics of microbicides combined with a contraceptive for multipurpose prevention; and microbicides combined with antimicrobial agents to simultaneously prevent HIV and other sexually transmitted infections (STIs). Microbicide formulations and new technologies that enhance adherence, such as injectable products, nanofibers and particles, ARV-containing films, and intravaginal rings also are being developed and studied.

Budget Policy:

The FY 2016 President's Budget request for Microbicides research is $113.072 million, an increase of $4.723 million or 4.4 percent above the FY 2015 Enacted level for this area of prevention research. In FY 2016, NIH will continue to support the discovery, design, development, formulation, and evaluation of microbicide candidates and the maintenance of a robust pipeline that includes both ARV and non-ARV products. Key ongoing activities include support for the NIH-funded Microbicide Trials Network (MTN); the integration of behavioral and social sciences research with clinical studies to better understand issues of adherence; and the necessary infrastructure to conduct basic, behavioral, social sciences and clinical microbicides research. 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 and the formulation of biomarkers to assess product adherence. Research also will focus on the development and testing of multi-purpose prevention technologies (MPTs) that prevent HIV and other sexually transmitted infections 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.

Behavioral and Social Science: As studies continue to define a role for the use of ARV 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. The HIV Care Continuum, sometimes called the HIV treatment cascade, is a model used to identify issues and opportunities related to improving the proportion of HIV-infected individuals who are engaged at each stage of HIV care -- from diagnosis to linkage to care, retention in care, receipt of appropriate ARV treatment, and achieving viral suppression. 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 also will continue to develop new research methods. These include approaches to increase recruitment into clinical trials; to enhance statistical analyses of behaviors, such as alcohol use, that can affect medication studies; to utilize means to optimize ongoing research in light of emerging results; and to identify behavioral issues relevant to genetic or genomic studies. NIH will also continue to foster the integration of biomedical and behavioral strategies in clinical investigations.

Budget Policy:

The FY 2016 President's Budget request for Behavioral and Social Science is $423.038 million, an increase of $8.165 million or 2.0 percent above the FY 2015 Enacted level. NIH will continue to 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. Increased attention will be given to research to improve the implementation of new prevention and therapeutic strategies in specific populations and social contexts. Research to address issues of stigma and to improve access to prevention and treatment resources will be supported, and a strong emphasis on basic science to understand both the social and biomedical (e.g., neurophysiologic and genomic) factors related to risk behaviors. 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 (Basic Science): 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, diagnostic methods, and tools for monitoring disease progression and the safety and effectiveness of antiviral therapies. Ground-breaking strides have been made toward 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. Research is also needed to examine the host microbiome as well as the genetic determinants associated with HIV susceptibility, disease progression, and treatment response. 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 2016 President's Budget request for the basic research area of Etiology and Pathogenesis is $698.310 million, an increase of $27.783 million or 4.1 percent above the FY 2015 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, the interplay between the host microbiome and HIV, 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. A key component of the NIH HIV cure research initiative will focus on studies on viral persistence, latency, and reactivation.

Program Portrait: The NIH HIV Cure Research Initiative

FY 2015 Level:	$ 127.3 million
FY 2016 Level:	$ 149.1 million
Change:	$+ 21.8 million

Research related to the potential for a cure or lifelong remission of HIV infection is a key NIH research priority, which involves research across a number of scientific areas. Although combination ARV therapy has changed the face of HIV infection by improving health, prolonging life, and substantially reducing the risk of HIV transmission, research toward a cure is a high priority for NIH because of the continued risks for HIV-associated clinical complications even with ARV use, the side effects of the drugs, and because the need for lifelong ARV therapy is in itself a heavy burden on HIV-infected persons. The experience of Timothy Ray Brown, the so-called "Berlin Patient" has demonstrated that a cure for HIV infection is possible. Subsequent research has shown that cure or lifelong HIV remission will be a difficult goal to achieve. Yet the same research has demonstrated that prolonged and sustained HIV remission with concomitant absence of chronic immune activation may be possible off ARV therapy, even if cure or lifelong remission has not yet been achieved apart from in the case of the Berlin Patient. Better understanding is needed of the mechanisms and dynamics of HIV latency, persistence, reactivation and reservoir formation in moving toward a therapeutic intervention that reliably and reproducibly results in a cure for HIV. Research on potential biomarkers for sustained viral remission and/or elimination, and biomarkers for incipient viral reactivation, among others, are also especially needed. Continued work is vital on therapeutic interventions for inducing sustained viral remission. The Initiative will help accelerate the ongoing development of drugs and cell and gene/gene modification-based therapeutic interventions that target persistent viral reservoirs in various cells, tissues, and organ systems, including in the central nervous system. NIH will also continue to support preclinical and clinical trials of innovative cure strategies including those incorporating therapeutic vaccines and anti-HIV monoclonal antibodies. More must be learned about the nature of long-lived tissue and cellular reservoirs of latent HIV and the factors affecting HIV rebound following cessation of antiretroviral therapy. Research into new mathematical, cellular, and animal models is also supported under this initiative.

Therapeutics

Drug Discovery, Development, and Treatment: Antiretroviral (ARV) treatment has resulted in profound immune recovery and enhanced function in patients who are able to adhere to prescribed HIV treatment regimens and tolerate the side effects and toxicities associated with ARV drugs. With the expansion of the classes of ARV available, the regimens required to provide viral suppression have been greatly simplified. ARV treatment has not only delayed the progression of HIV disease to AIDS, it has been increasingly effective at prolonged viral suppression and delayed development of viral resistance. The addition of integrase inhibitors to the ARV arsenal has enhanced treatment options for the treatment experienced, and novel

options for greater virologic control for the treatment naïve. Unfortunately, the challenge continues to be the ongoing morbidity and mortality associated with the complications of long-term HIV infection, including but not limited to tuberculosis, Hepatitis B and C, metabolic dysregulation due to HIV infection and its treatment, as well as AIDS- and non-AIDS defining cancers. The development of the directly acting agents has also significantly changed the impact of Hepatitis C, with more effective agents that can achieve a sustained virologic response in over 90 percent of treated individuals. Nevertheless, the impact of HIV on the reservoirs beyond the reach of antiretrovirals and the progression of renal and hepatic disease unresponsive to treatment remains a significant source of morbidity and mortality for those living with HIV infection, especially those who are from marginalized segments of the population with limited access to care. 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 an 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 the HIV cure research initiative 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.

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.

***Therapeutics as Prevention*:** A critical 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, helping to establish the

foundation for the clinical guidance for the widespread use of PrEP. 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 for potential new PrEP strategies; test PrEP in high risk uninfected populations, including adolescents; evaluate post-exposure prophylaxis, the use of ARV 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 2016 President's Budget request for Therapeutics research is $760.125 million, an increase of $14.572 million or 2.0 percent above the FY 2015 Enacted level. Funds will be provided to support high priority research on treatment and prevention of HIV-associated co-infections and co-morbidities; and basic research studies targeting and eradicating HIV reservoirs. Resources will be directed to support: studies of the comparative immunology and molecular oncology of HIV-associated lymphomas; research on AIDS- and non-AIDS defining cancers, especially among older persons with HIV infection; delineating the role of immune activation and residual inflammation and microbial translocation in chronic HIV infection; research on the interaction of aging and neuro-AIDS; development of new strategies to test and treat patients with HIV-related co-infections, including Hepatitis C virus and tuberculosis; conducting clinical studies on cardiovascular and other metabolic complications of HIV disease and ART; treatment of aging HIV-infected individuals to prevent transmission and reduce HIV-associated morbidity and mortality; identifying new drug targets based on the structure of HIV/host complexes; identifying neurobehavioral and neurocognitive factors that result from HIV infection or are modified by HIV infection; and support for strategies to increase HIV testing and linkage to care in adolescent populations. Within the NIH HIV Cure initiative, funds will be provided for expansion of programs targeting innovative approaches to develop and evaluate novel approaches to control and eradicate HIV infection that may lead to a cure; identifying innovative approaches to quantify the latent HIV reservoirs; and novel strategies for targeting the central nervous system viral reservoir without inducing reactivation. Funds also will support research on the discovery and testing of new combinations of ARVs and sustained release formulations and delivery systems that may be used in potential new strategies for treatment and prevention that support adherence, minimize side effects, and maintain viral suppression.

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 United States are identifying new HIV-related co-morbidities and helping to differentiate effects related to long-term ARV treatment from those related to HIV disease and chronic co-morbidities. As the AIDS epidemic continues to evolve, there is a crucial need for carefully

designed 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 United States; 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 United States 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 2016 President's Budget request for Natural History and Epidemiology is $236.868 million, an increase of $6.431 million or 2.8 percent over the FY 2015 Enacted level.

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 of its treatment are critically important at the current stage of the HIV epidemic as are 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 treatment and prevention cascades through 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 to evaluate the economic impact and cost-effectiveness of various intervention 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 global expansion of the NIH-funded HIV research has necessitated the development of research training, and infrastructure and capacity building efforts in many resource-limited settings throughout the world. The 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 United States. 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 2016 President's Budget estimate for Training, Infrastructure, and Capacity Building is $264.978 million, an increase of $7.387 million or 2.9 percent above the FY 2015 Enacted level. NIH will continue to support training programs and infrastructure development for both U.S.-based and international researchers to build the critical capacity to conduct AIDS research in the United States and in developing countries, including capacity for ongoing efforts to increase the supply of non-human

primates and develop other animal models for AIDS research. 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, particularly to issues related to adherence to prescribed treatments and prevention strategies, 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 United States 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 2016 President's Budget estimate for Information Dissemination is $35.723 million, an increase of $0.394 million or 1.1 percent above the FY 2015 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. 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. The NIH AIDS research studies are designed so that the results are relevant for both the host nation and the United States. 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 2014 Actual	FY 2015 Enacted	FY 2016 PB
$453.577	$ 451.199	$462.240

Benefits of AIDS Research to Other Areas: The NIH investment in AIDS research has resulted in critical scientific accomplishments that benefit not only the 35 million HIV-infected individuals around the world, but has also contributed knowledge to the prevention, diagnosis, and treatment of many other diseases and conditions. AIDS research deepens the overall 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 immunology and biology research has informed the understanding of inflammation and aging. Research on HIV-associated neurologic and cognitive manifestations ultimately will benefit millions of patients with Alzheimer's disease and other aging and dementia issues. AIDS treatment research has led to more effective drugs for multiple bacterial, mycobacterial, and fungal diseases and fostered significant improvements in drug design and delivery technologies that can improve adherence; and led to the development of curative regimens for Hepatitis C, which affects about 150 million people globally. 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 the more than 28,000 Americans who receive an organ transplant each year. 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 NIH's 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 United States national commitment to AIDS research remains strong. 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 global epidemic so that we can all once again live in a world without AIDS.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Resource Summary

	Budget Authority (in Millions)		
	FY 2014 Final	FY 2015 Enacted	FY 2016 Request
Drug Resources by Function			
Research and Development: Prevention	$391.620	$389.478	$401.473
Research and Development: Treatment	$685.691	$685.761	$707.143
Total Drug Resources by Function	**$1,077.311**	**$1,075.239**	**$1,108.616**
Drug Resources by Decision Unit			
National Institute on Drug Abuse	$1,017.961	$1,015.705	$1,047.397
National Institute on Alcohol Abuse and Alcoholism	59.350	59.534	61.219
Total Drug Resources by Decision Unit	**$1,077.311**	**$1,075.239**	**$1,108.616**

Drug Resources Personnel Summary			
Total FTEs (direct only)	393	395	395
Drug Resources as a Percent of Budget			
Total Agency Budget (in Billions)	$30.1	$30.1	$31.1
Drug Resources Percentage	3.4%	3.4%	3.4%

Program Summary

MISSION

The National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two of the twenty-seven Institutes and Centers (ICs) of the National Institutes of Health (NIH), support the National Drug Control Strategy: NIDA, by funding research on the prevention and treatment of substance abuse, addiction and its harmful consequences; and NIAAA, by funding research on the prevention and treatment of underage drinking and its harmful consequences.

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 use disorders in this country and worldwide.

In addition, NIDA is supporting research to better understand the impact of changes in state policies related to marijuana. Current research is exploring the impact on trends in use, harm perception, health consequences including trauma and death from car accidents, and educational outcomes, particularly for adolescents and young adults. In addition, a significant new initiative is being initiated as part of the Collaborative Research on Addiction (CRAN), a trans-NIH consortium involving NIDA, NIAAA, and the National Cancer Institute (NCI), and in partnership with the *Eunice Kennedy Shriver* National Institute of Child Health and Health Development (NICHD), that will seek to understand the impact of marijuana (and other drug) use during adolescence. This Adolescent Brain Cognitive Development (ABCD) study will be the largest longitudinal brain-imaging study of adolescents ever conducted. It will follow approximately 10,000 U.S. adolescents for 10-12 years to determine whether use of marijuana, alcohol, nicotine, or other drugs is associated with changes in brain function and behavior throughout development. Participants will be recruited prior to any substance use and will periodically undergo a variety of tests such as brain imaging, genetic, psychiatric, and cognitive testing to potentially identify predictors of adolescent substance misuse and to delineate the role of social, psychological, and biological mechanisms.

Alcohol misuse has profound effects on the health and well-being of individuals, families, and communities, with substantial economic costs. Since its creation, NIAAA has led the national effort to define alcohol problems as medical in nature and address them using evidence-based findings. The research supported by the Institute has transformed our understanding of alcohol misuse and its consequences, as well as their treatment. NIAAA is working to reduce the considerable burden of alcohol misuse for individuals at all stages of life by supporting: research on the neurobiological mechanisms underlying alcohol use disorder (AUD) and co-occurring disorders; the development of behavioral therapies and medications that promote recovery; studies on the consequences of alcohol misuse, including fetal alcohol spectrum disorders (FASD), effects on the developing adolescent brain, and tissue and organ damage; the development of strategies to prevent and intervene with the short- and long-term consequences of alcohol misuse; the translation and implementation of research findings into improved health care for individuals with AUD alone and with co-occurring conditions; and the dissemination of research-based information to health care providers, researchers, policy makers and the public.

METHODOLOGY

NIDA's entire budget is drug-related and 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 and binge drinking in minors (children under the legal drinking age of 21), as well as the negative consequences of alcohol use, e.g. alcohol-related injuries, impact on adolescent development, including on the developing brain, and the

development of alcohol use disorder. It includes basic research, epidemiological studies, behavioral research, screening and intervention studies and development and testing of preventive interventions. NIAAA's methodology for developing budget estimates 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 2016 Request is $1,108.6 million for NIH's drug-related activities, which is an increase of $33.4 million above the FY 2015 enacted 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 substance use disorders, 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 disorders, HIV, or both, into a network of care and generate a major public health impact.

National Institute on Drug Abuse
FY 2016 Request: $1,047.4 million
(Reflects $31.7 million increase over FY 2015)

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).

Epidemiology, Services and Prevention Research (FY 2016 Request: $265.8 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 to monitor drug-related issues and trends locally and nationally, such as the emergence of synthetic drugs and e-cigarettes. It also supports a large research network for conducting studies related to treatment of substance use disorders (SUDs) in the criminal justice system, including studies that pertain to the

implementation of medication-assisted treatment (MAT) and seek, test, treat, and retain (STTR) for substance abusers at risk for HIV. Program efforts also help identify substance abuse trends locally, nationally, and internationally; guide development of responsive interventions for a variety of populations; and encourage optimal implementation and service delivery in real-world settings. For example, NIDA recently launched an innovative National Drug Early Warning System (NDEWS) to monitor emerging trends related to illicit drug use and to identify increased use of designer synthetic compounds. NDEWS will generate critical information about new drug trends in specific locations around the country so that rapid, informed, and effective public health responses can be developed and implemented precisely where and when they are needed. NIDA is also supporting research to better understand the impact of policy changes related to substance use including implementation of health reform and changes in state policies related to marijuana. Specifically, current research is evaluating: 1) the impact of health reform on access to quality treatment for persons with SUDs, and 2) the longer-term outcomes resulting from changes in State marijuana policies such as trends in use, harm perception, health consequences including trauma and death from car accidents, and educational outcomes, particularly for adolescents and young adults. Such knowledge can be then used to inform policy and to improve prevention and treatment interventions.

Basic and Clinical Neuroscience Research (FY 2016 Request: $446.6 million)

The Basic and Clinical Neuroscience portfolio seeks to expand our understanding of the fundamental neurological, genetic/epigenetic, and behavioral processes that underlie SUDs. Central to this goal are efforts to tease apart the multiple factors that contribute to drug abuse and addiction risk, with particular attention to significant individual differences in risk and responses to drugs, while at the same time expanding our basic knowledge of the function of the brain from the molecular to the behavioral. Key projects are investigating the effects of drugs on gene expression and brain development and function, and exploring gender-related differences in these effects. Risk for addiction is profoundly affected by an individual's genes as well as environmental conditions, such as stress and early exposure to drugs of abuse. Additional studies are exploring the mechanisms underlying these effects, including the role of epigenetic changes that can influence long-term patterns of gene expression in specific brain cells (neuron and glia) without changing DNA sequence. Collectively, this research will improve our understanding of the basic neural and genetic mechanisms that underlie drug abuse and addiction and will provide critical insights toward the development of more effective approaches for the prevention and treatment of SUDs. For example, continuing efforts to improve our understanding of the endocannabinoid system are opening up new areas of investigation for the development of novel pain and addiction treatments. Other projects are exploring the basic processes underlying resilience against SUDs in childhood and adolescence. In addition, and in line with the goals of the President's Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, NIDA is supporting research to: 1) develop advanced technologies that improve our ability to study the organization and function of the living brain; 2) better understand the interactions of complex neural circuits including those that mediate reward, aversion to drug effects, and related decision making through development; and 3) develop strategies to therapeutically influence SUD-relevant brain circuits (e.g., transcranial magnetic and deep brain stimulation, neurofeedback, optogenetics).

Progress in these combined areas will revolutionize our ability to mitigate or even reverse the deleterious effects of addiction.

Pharmacotherapies and Medical Consequences (FY 2016 Request: $137.5 million)
Since the pharmaceutical industry has had limited involvement in the development of medications for SUDs, the responsibility for their development has rested largely with NIDA. NIDA, therefore, has developed a program that is responsible for medications development for SUDs. To leverage NIDA resources, this program encourages the formation of alliances between strategic partners (such as academic institutions, pharmaceutical and biotechnology companies) with the common goal of advancing medications through the development pipeline toward FDA approval in a timely manner. NIDA conducts research to decrease the risk associated with medications development to make it more appealing for pharmaceutical companies to complete costly phase IIb and III clinical studies. An example of such a project is a partnership with AstraZeneca to explore a novel medication that modulates the activity of glutamate – an excitatory neurotransmitter – to treat drug addiction. Preclinical studies with this class of molecules indicate that it could be effective for treating abuse of various drugs such as tobacco and cocaine. Another example is the partnership with two biotechnology companies to support the development of an intranasal formulation of naloxone (see program portrait on intranasal naloxone). In addition, NIDA is collaborating with Teva Pharmaceutical Industries on a clinical trial to test the efficacy and safety of a cholinesterase compound that has shown promise in pre-clinical trials for the treatment of cocaine addiction. NIDA also hosted a conference bringing together basic and translational researchers along with representatives from the pharmaceutical industry to evaluate emerging targets for stimulant use disorders and to identify ways to accelerate this area of research. NIDA is also continuing to invest in research supporting the development of vaccines and antibodies for the treatment of SUDs. A lingering challenge in this area has been the development of vaccines that stimulate an immune response powerful enough to neutralize high concentrations of a drug before it enters the brain.

Clinical Trials Network (CTN) (FY 2016 Request: $45.9 million)
CTN comprises 13 research nodes and more than 240 community treatment programs and/or medical settings 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 SUDs and related disorders, such as comorbid mental health disorders and HIV, with diverse patient populations and community treatment providers. The CTN is currently conducting studies evaluating: 1) a comparison of Vivitrol® (naltrexone for extended-release injectable suspension) to Suboxone® (buprenorphine and naloxone) Sublingual Film for patients addicted to heroin or other opioids, including prescription pain relievers; 2) N-acetylcysteine for treatment of marijuana addiction; 3) a combination therapy with Vivitrol® plus Wellbutrin XL® (bupropion hydrochloride, Extended-release Tablets) for treatment of methamphetamine addiction; 4) Vivitrol® for HIV-positive opioid users in HIV settings; and 5) and a brief screening and assessment instrument to identify patients with SUDs in general medical settings.

Intramural Research Program (IRP) (FY 2016 Request: $89.0 million)

IRP performs cutting-edge research within a coordinated multidisciplinary framework to: 1) elucidate the nature of the addictive process; 2) determine the potential use of emerging new therapies for SUDs, 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. For example, IRP is furthering substance abuse research through the recently established Designer Drug Research Unit (DDRU), which was created in response to the worldwide epidemic of synthetic drug use. Synthetic drugs are marketed as safe, cheap, and legal alternatives to illicit drugs like marijuana, cocaine, and MDMA (a.k.a. Ecstasy). However, they can produce serious cardiovascular and neurological consequences that 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. 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. Similarly, IRP is working to develop and evaluate quicker, more reliable, and more accurate roadside tests for drug-related intoxication. With the legalization of recreational or medical marijuana use in some states, this is a critically needed tool for enforcing drug-impaired driving laws. IRP has also established a Medications Development Program that works with NIDA's Extramural Division of Pharmacotherapies and Medical Consequences of Drug Abuse, NIAAA, the National Center for Advancing Translational Sciences (NCATS), and the Brain Science Institute, Johns Hopkins University School of Medicine, to identify potential targets for addiction medication development. In addition, IRP is working to develop advanced new technologies to genetically manipulate and study the organization and function of brain circuits involved in SUDs.

Research Management and Support (RMS) (FY 2016 Request: $62.6 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 1,600 research grants and more than 130 research and development contracts. In addition to the infrastructure required to support research and training, NIDA also strives to provide evidence-based resource and educational materials about SUDs and to raise awareness of the science relating to cutting-edge issues such as marijuana research, opioid overdose prevention, and Medication Assisted Treatments.

In addition, NIDA's Office of Science Policy and Communication (OSPC) leads strategic efforts to inform public health policy and practice by ensuring the institute is the primary trusted source for scientific information on drug abuse and addiction. Healthcare providers are a key target audience for NIDA's outreach efforts. NIDA leads the NIH Pain Consortium Centers of Excellence in Pain Education (CoEPEs); these twelve centers work to enhance patient outcomes by improving the education of healthcare professionals about pain and its treatment. The CoEPEs act as hubs for the development, evaluation, and distribution of pain management

curriculum resources for medical, dental, nursing and pharmacy schools to improve how health care professionals are taught about pain and its treatment.

National Institute of Alcohol Abuse and Alcoholism

FY 2016 Request: $61.2 million

(Reflects $1.7 million increase over FY 2015)

A key priority for NIAAA is preventing and reducing underage drinking. NIAAA recognizes the pervasive use of alcohol among young people and its negative consequences, as well as 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 disorder in children and adolescents, and to identify risk for alcohol use, especially for younger children. NIAAA launched an initiative to evaluate the guide in practice and is supporting six studies that are evaluating the guide in a range of settings: one in a network of emergency departments; one in a juvenile justice setting; two in primary care; one with youth who have a chronic condition (e.g., asthma, diabetes); and one in a school setting The brief, two-question screener is being assessed in youth ages 9-18 as a predictor of alcohol risk, alcohol use, and alcohol problems including alcohol use disorder, and as an initial screen for other behavioral health problems; for example, other drug use, smoking, or conduct disorder. NIAAA's investment in underage drinking research also includes the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a longitudinal study that is following more than 800 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. NIAAA's NCANDA program has created the foundation for a more extensive longitudinal study under the CRAN initiative to assess the neurodevelopmental consequences of substance use in youth. NIAAA will continue to support complementary studies with animals under the Neurobiology of Adolescent Drinking in Adulthood initiative which investigates the effects of adolescent alcohol exposure on subsequent brain function and behavior into adulthood. Given that many college students who consume alcohol are underage, efforts to prevent and intervene with drinking by college students will continue to be a major NIAAA priority in FY 2016.

PERFORMANCE

Information regarding the performance of the drug control efforts of NIH is based on the agency's performance reporting in support of the budget process and other information that measures the agency's contribution to the *Strategy*. NIH's performance 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. Most measures are 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 2014.

NIDA and NIAAA support a number of trans-NIH measures in the Scientific Research Outcome (SRO) functional area. While NIDA and NIAAA engage in many research and related support activities, two measures best reflect the breadth of their portfolios, specifically, efforts in the prevention and treatment of substance abuse, addiction, and its consequences.
One of these measures is 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." This measure is indicative of NIDA's and NIAAA's efforts to support research to foster the development and implementation of prevention based strategies for reducing substance abuse and addiction. SRO-5.15 began in FY 2014 and replaces the previous prevention measure, SRO-3.5, which was completed in FY 2013." NIH's prevention portfolio encompasses a broad range of research on the efficacy and cost effectiveness of primary prevention programs—designed to prevent substance use before it starts, or prevent escalation to abuse or addiction— and how these programs can be enhanced by targeting prevention efforts toward populations with specific vulnerabilities (genetic, psychosocial, or environmental) that affect their likelihood of taking drugs or becoming addicted.

NIDA and NIAAA also contribute 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 2014 Target**	**FY 2014 Achieved**
» SRO-5.15 (started in FY 2014): 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.	Develop and assess at least two interventions to prevent drug use, drug use problems, and risk behaviors.	NIH funded research tested multiple interventions to prevent drug use, drug use problems, and drug related risky behaviors including HIV risk behaviors.
» 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.	Undertake analyses to examine the effects of implementation strategies used in MATICCE and HIV-STIC protocols.	Eight peer-reviewed publications analyzing the effects of implementation of the MATICCE and HIV-STIC protocols have been published. Several more manuscripts are in progress.

Prevention – SRO-5.15
NIDA continues to fund a robust theory-based prevention portfolio that builds upon solid epidemiological findings and insights from genetics and neuroscience and applies this

knowledge to development of effective strategies to prevent initiation of drug use and escalation of use to addiction in underage youth.

From FY 2014 to the present (FY 2015), multiple studies have been funded to develop and test interventions to prevent drug use, drug use problems, and risk behaviors. NIDA is currently supporting studies to test culturally and developmentally appropriate strategies to prevent substance use and abuse across the lifespan: for all developmental stages, from birth through adulthood and older age; for diverse racial/ethnic populations, targeted to diverse settings such as family, school, community, and health care settings; and for diverse special populations and/or high risk populations, such LGBT, homeless, child welfare involved, juvenile justice system involved, criminal justice involved, individuals comorbid conditions, populations at risk for HIV/AIDS.

In FY 2014 multiple publications were released related to this target by NIDA-funded researchers who conducted studies that tested interventions to prevent drug use, drug use problems, and risk behaviors. One recent study explored the effect of a Multidimensional Treatment Foster Care (MTFC) in at-risk female youth who had been referred for out-of-home placement due to chronic delinquency.[1] Previous studies have shown that juvenile justice girls have high rates of co-occurring risk behaviors including substance abuse. The current research showed that women with prior juvenile justice involvement who were assigned to the MTFC intervention during adolescence showed greater decreases in drug use than girls assigned to treatment as usual. In addition, women who participated in MTFC were found to be more resilient to partner drug use than women in the treatment as usual condition.

Another recent publication demonstrated that girls who participated in the Middle School Success (MSS) Intervention, a program to promote healthy adjustment in foster girls, showed lower levels of health risk-taking behaviors.[2] The analysis demonstrated that the effect of the intervention on health-risking sexual behavior was mediated through its effect on tobacco and marijuana use. These finding demonstrate that the MSS prevention intervention delivered during adolescence improves young adult drug use trajectories (7-9 years after the study began). These findings add to a growing body of evidence of the longer term impacts of early prevention interventions delivered during adolescence to a high risk population.

Another ongoing study is looking at the feasibility and effectiveness of using web-based tools for screening college students for marijuana use and providing brief interventions.[3] Students who use marijuana have an increased likelihood of poor academic performance, as well as physical health and relationships problems. Despite the availability of efficacious interventions,

[1] Rhoades KA et al. Drug Use Trajectories After a Randomized Controlled Trial of MTFC: Associations with Partner Drug Use. J Res Adolesc. 2014 Mar 1;24(1):40-54. PubMed PMID: 24729667

[2] Kim HK, et al. Intervention Effects on Health-Risking Sexual Behavior Among Girls in Foster Care: The Role of Placement Disruption and Tobacco and Marijuana Use. J Child Adolesc Subst Abuse. 2013 Nov 1;22(5):370-387. PubMed PMID: 24043921

[3] Palfai TP, et al. Web-based screening and brief intervention for student marijuana use in a university health center: pilot study to examine the implementation of eCHECKUP TO GO in different contexts. Addict Behav. 2014 Sep;39(9):1346-52.

few students identify their marijuana use as problematic or seek treatment to reduce their use. Recent developments in health technology have expanded the range of tools available to engage students in screening and to deliver interventions. A pilot study was conducted to explore the efficacy of a web-based screening and brief intervention tool that delivers personalized feedback in an easily utilized and confidential manner to students presenting their marijuana use to a university health center. The researchers found that while the intervention did not reduce frequency of marijuana use the intervention significantly altered perceived norms regarding marijuana use. The findings demonstrated that it is feasible to screen and identify marijuana users in a college student health center and deliver a web-based intervention. The study suggests that these types of technology based intervention can be useful for correcting misperceptions of norms and reducing related consequences.

Collectively these findings further support key prevention lessons and principles that have emerged from NIDA funded studies: prevention interventions implemented in early childhood have effects in later developmental stages and into young adulthood; universal interventions can have strong effects in higher risk youth; universal substance use prevention interventions can have effects on other behavioral outcomes, beyond those specifically targeted by the intervention (e.g. , social services utilization).

Treatment - SRO-8.7

NIDA funds a broad portfolio of research addressing drug abuse in the context of the criminal justice system. From 2002-2014 NIDA funded the Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) program, a multisite research cooperative. The CJ-DATS program aligned with NIDA's multi-pronged approach to rapidly move more promising science-based addiction treatments into community settings, to improve existing drug treatment for criminal justice populations, and to inform the development of integrated treatment models. The CJ-DATS program included testing of *Medication-Assisted Treatment Implementation in Community Correctional Environments (MATICCE) and HIV Services and Treatment Implementation in Corrections (HIV-STIC).* The MATICCE protocol tested implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies. The HIV-STIC protocol tested an organizational intervention strategy targeting effective implementation of quality improvements in HIV services for preventing, detecting, and treating HIV in offenders under correctional supervision. Through these studies CJ-DATS contributed to a significant body of research describing existing treatment practices in the criminal justice system, developing and testing the effectiveness of specific interventions, and exploring strategies for implementation, quality improvement, and of drug abuse treatment programs for criminal justice populations.

The CJ-DATS research protocols developed in FY 2010 to test the two implementation models – MATTICCE and HIV-STIC – completed data collection in FY 2014. Across the two protocols

described below, 8 peer-reviewed publications have been published to date[4,5,6,7,8,9,10,11]. More than a dozen additional manuscripts are in progress.

MATICCE was a collaborative study involving nine academic research centers (RCs), each with two community corrections partner agencies. The MATICCE protocol tested implementation approaches aimed at improving service coordination between community correctional agencies and local treatment agencies. The goals were to increase the number of persons in corrections who are given access to medication-assisted treatment (MAT) and to improve community corrections agents' knowledge and perceptions about MAT and increase their intent to refer individuals to appropriate community-based MAT services. The study randomized correctional agencies to one of two implementation strategies: 1) a KPI (Knowledge, Perception, and Information) intervention where correctional staff received structured training on use of medications in addiction treatment, including the effectiveness of MAT for reducing drug use and crime, for overcoming negative perceptions about MAT, and for providing information about local healthcare providers offering MAT; or 2) the KPI training plus an Organizational Linkage (OL) intervention, which engages key representatives from the corrections and treatment agencies in a strategic planning process designed to facilitate inter-organizational referral relationships, thereby improving the flow of offenders from community corrections to community-based treatment.

One peer-reviewed publication reporting on results of the MATICCE program is currently in press. This publication reports that the KPI staff training coupled with the facilitated OL strategic planning intervention was more effective than staff training alone in improving probation and parole officers' acceptance of MAT and willingness to refer clients to treatment. There are currently two additional publications related to the MATICCE study undergoing peer review and five being prepared for submission.

HIV-STIC was a collaborative study involving 9 academic research centers (RCs) and 30 community corrections partner agencies. The HIV-STIC protocol tested an organizational intervention strategy targeting effective implementation of quality improvements in HIV

[4] Pearson, F., et al. (2014).Efficacy of a process improvement intervention on delivery of HIV services: A multi-site trial. American Journal of Public Health.
[5] Visher, C., et al. (2014). The effect of a local change team intervention on staff attitudes toward HIV service delivery in correctional settings: A randomized trial. AIDS Education and Prevention, 25:5, 411-428.
[6] Gordon, M., et al. (2014). Buprenorphine treatment for probationers and parolees. Substance Abuse. DOI: 10.1080/08897077.2014.902787
[7] Swan, H., et al. (In press, 2015). Improvements in correctional HIV services: A case study in Delaware. Journal of Correctional Health Care. Special Issue 21(2).
[8] Belenko, S., et al. (2013). Policies and practices in the delivery of HIV services in correctional agencies and facilities: Results from a multi-site survey. Journal of Correctional Health Care, 19(4), 293-310.
[9] Ducharme, L.J., et al. (2013). Implementing drug abuse treatment services in criminal justice settings: Introduction to the CJ-DATS study protocol series. Health & Justice, 1:5.
[10] Friedmann, P.D., et al. (2013). A cluster randomized trial of an organizational linkage intervention for offenders with substance use disorders: Study protocol. Health & Justice, 1:6.
[11] Belenko, S., et al. (2013). A cluster randomized trial of utilizing a local change team approach to improve the delivery of HIV services in correctional settings: Study protocol. Health & Justice, 1:8.

services for preventing, detecting, and treating HIV in offenders under correctional supervision. The study randomized correctional facilities to one of two conditions. A control received basic training on the fundamentals of HIV infection, prevention, testing, and treatment, as well as information about the HIV services continuum. The experimental group implemented a process improvement approach to guide a Local Change Team (LCT) through a structured series of steps to improve HIV services. Such models have been found to improve health services implementation in other settings, but had not previously been tested in correctional settings or with HIV services.

Multiple peer-reviewed publications were released in 2014 demonstrating that the modified NIATx (Network for Improvement of Addiction Treatment) process improvement model used by the HIV-STIC protocol was successful in increasing the likelihood that a correctional facility would successfully deliver HIV services to their inmates as compared to facilities that only received training on HIV services.[12] The process improvement model also resulted in more positive attitudes toward HIV service delivery among correctional staff.[13] A survey of sites participating in the CJ-DATS HIV-STIC protocol prior to study commencement indicated that there was wide variation in the degree to which these correctional facilities adhered to national guidelines around HIV prevention, detection and care.[14] Gaps in HIV service delivery were primarily attributed to limited resources. Five additional publications related to HIV-STIC are currently in development.

In July 2013 NIDA launched the Juvenile Justice Translational Research on Interventions for Adolescents in the Legal System (JJ-TRIALS) program. JJ-TRIALS is a seven-site cooperative research program designed to identify and test strategies for improving the delivery of evidence-based substance abuse and HIV prevention and treatment services for justice-involved youth. Many evidence-based interventions targeting adolescent substance abuse and HIV screening, assessment, prevention, and treatment currently exist. Unfortunately, implementation of these interventions within juvenile justice settings is variable, incomplete, and non-systematic at best. This research program will provide insight into the process by which juvenile justice and other service settings can successfully adopt and adapt existing evidence-based programs and strategies to improve drug abuse and HIV service delivery for at-risk youth. The cooperative will also conduct a nationally representative survey of the juvenile justice system that will provide information about policies and practices related to substance use assessment and service delivery in these settings across the United States.

NIDA is also supporting the Seek, Test, Treat, and Retain (STTR) Initiative to empirically test the STTR paradigm with drug abusers in criminal justice populations. Researchers are developing,

[12] Pearson, F., et al. (2014). Efficacy of a process improvement intervention on delivery of HIV services: A multi-site trial. American Journal of Public Health.
[13] Visher, C., et al (2014). The effect of a local change team intervention on staff attitudes toward HIV service delivery in correctional settings: A randomized trial. AIDS Education and Prevention, 25:5, 411-428
[14] Belenko, S., et al. (2013). Policies and practices in the delivery of HIV services in correctional agencies and facilities: Results from a multi-site survey. Journal of Correctional Health Care, 19(4), 293-310.

implementing, and testing strategies to increase HIV testing and the provision of HAART to HIV positive individuals involved with the criminal justice system, with particular focus on continuity of HAART during and after community re-entry following incarceration. (HAART, or highly active antiretroviral therapy, is a customized combination of different classes of medications that a physician prescribes based on such factors as the patient's viral load (how much virus is in the blood), the particular strain of the virus, the CD4+ cell count, and other considerations (e.g., disease symptoms).)

Research Highlights

Decreased dopamine signaling in the striatum leads to escalation of cocaine use in rats

Drug addiction is a neuropsychiatric disorder marked by escalating drug use. Dopamine neurotransmission in the ventromedial striatum (VMS) (part of the brain reward system) mediates the acute reinforcing effects of abused drugs, but with prolonged use the dorsolateral striatum is thought to assume control over drug seeking. NIDA supported researchers[15] measured dopamine release in these brain regions during a cocaine self-administration experiment that produced escalation of drug-taking in rats. Surprisingly, they found that the typical rapid, phasic bursts of dopamine decreased in both regions as the rate of cocaine intake increased. The decrement in dopamine in the VMS was significantly correlated with the rate of escalation of drug use. Administration of a drug that replenished dopamine signaling, the dopamine precursor L-DOPA, in the VMS reversed escalation of drug use demonstrating a causal relationship between lower dopamine release and excessive drug use. These data provide new mechanistic and therapeutic insights into the excessive drug intake that occurs following chronic use.

Baseline cognitive inhibitory task performance predicts subsequent substance use behaviors

Adolescent substance use has been associated with poorer neuropsychological functioning, but it is unclear if deficits predate or follow the onset of use. A recent prospective study[16] sought to understand how neuropsychological functioning during early adolescence could predict substance use by late adolescence. Participants included 175 substance-use-naïve healthy 12- to 14-year-olds recruited from local schools who completed extensive interviews and neuropsychological tests. Each year, participants' substance use was assessed. By late adolescence (ages 17 to 18), 105 participants transitioned into substance use and 75 remained substance-naïve. The study examined how baseline cognitive performance predicted subsequent substance use, controlling for common substance use risk factors (i.e., family history, externalizing behaviors, gender, pubertal development, and age). Poorer baseline performance on tests of cognitive inhibition-interference predicted higher measures of drinking and marijuana use by ages 17 to 18. Performances on short-term memory, sustained attention,

[15] Willuhn et al. Excessive cocaine use results from decreased phasic dopamine signaling In the striatum. Nat Neurosci. 17(5):704-9 (2014).

[16] Squeglia LM. Et al. Inhibition during Early Adolescence Predicts Alcohol and Marijuana Use by Late Adolescence. Neuropsychology 28(5):782-90 (2014).

verbal learning and memory, visuospatial functioning and spatial planning did not predict subsequent substance use behavior. Inhibitory functioning measures could help identify teens at risk for initiating heavy substance use during adolescence, and potentially could be modified to improve outcome.

Early onset marijuana use associated with white matter abnormalities and higher impulsivity

Adolescence is a critical period of active brain development, teens and emerging adults are at greater risk for experiencing the negative effects of marijuana (MJ) on the brain. A recent study[17] examined the relationship between age of onset of MJ use, white matter microstructure, and reported impulsivity in chronic, heavy MJ smokers. Twenty-five MJ smokers and 18 healthy controls underwent diffusion tensor imaging and completed a standard Impulsiveness Scale (Barratt). MJ smokers were also divided into early onset (regular use prior to age 16) and late onset (age 16 or later) groups in order to clarify the impact of age of onset of MJ use on these variables. MJ smokers exhibited alterations in white matter microstructure (significantly reduced 15 fractional anisotropy (FA) relative to controls) as well as higher levels of impulsivity. Earlier MJ onset was associated with greater white matter alterations. Interestingly, within the early onset group, higher impulsivity scores were correlated with lower FA, a relationship that was not observed in the late onset smokers. MJ use is associated with altered white matter development and reported impulsivity, particularly in early onset smokers.

Impact of marijuana legalization in Colorado on perceived risk of marijuana's harms

In 2009, policy changes were accompanied by a rapid increase in the number of medical marijuana cardholders in Colorado. A recent study[18] using the National Survey on Drug Use and Health tested for temporal changes in marijuana attitudes and marijuana use related outcomes in Colorado (2003-11) and differences between Colorado and thirty-four non-medical marijuana states (NMMS). The authors of this study tested whether patterns seen in Colorado prior to (2006-8) and during (2009-11) marijuana commercialization differed from patterns in NMMS while controlling for demographics. Within Colorado the percentage of individuals perceiving "great-risk" to using marijuana 1-2 times per week dropped significantly in all age groups studied between 2007-8 and 2010-11 (from 45% to 31% among those 26 years and older). By 2010-11 past-year marijuana abuse and dependence had become more prevalent in Colorado for 12-17 year olds (5% vs 3% in NMMS) and 18-25 year olds (9% vs. 5%). Analyses demonstrated significantly greater reductions in perceived risk among those 26 years and older and marijuana abuse/dependence among 12-17 year olds in Colorado compared to NMMS in more recent years (2009-11 vs. 2006-8). These results show that commercialization of marijuana in Colorado has been associated with lower risk perception. Evidence is suggestive of an association with increased marijuana abuse/dependence. Analyses including subsequent years, once available, will help determine whether such changes represent momentary vs. sustained effects.

[17] Gruber SA et al. Worth the wait: effects of age of onset of marijuana use on white matter and impulsivity. Psychopharmacology. 231(8):1455–1465 (2014)

[18] Schuermeyer J. et al. Temporal trends in marijuana attitudes, availability and use in Colorado compared to non-medical Marijuana States: 2003-11.Drug Alcohol Depend. 140:145-55 (2014).

Buprenorphine taper is less effective than maintenance in treatment of opioid use disorders

Prescription drug abuse in the United States and elsewhere in the world is increasing at an alarming rate with non-medical opioid use increasing to epidemic proportions over the past two decades. It is imperative to identify and effectively treat individuals with opioid use disorders, however evidence-based medication assisted treatment strategies are often not provided or are restricted in ways that decrease their efficacy. A recent investigation[19] explored outcomes associated with tapering patients off of buprenorphine, a partial opioid agonist, over a nine-week period of time (after six weeks of stabilization) compares to patients maintained on the medication. The study concluded that maintenance buprenorphine therapy is more effective than tapering and discontinuation of the medication in treating prescription opioid-dependent patients in primary care settings. The results suggest that buprenorphine taper should be used only when it is clinically indicated in the treatment of patients dependent on prescription opioids. Additional research is needed to help identify factors associated with successful tapering and maintenance therapy.

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2014 Target**	**FY 2014 Achieved**
» 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	Develop materials for dissemination to academic officials that help them address underage and harmful drinking and other substance use by their students.	NIH developed a research-based decision tool, the NIAAA College Alcohol Interventions Matrix (CollegeAIM), to help colleges and universities select appropriate strategies to meet their alcohol intervention goals.
» 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.	Support research to evaluate the effectiveness of the underage drinking screening guide as a predictor of alcohol risk, alcohol use, and related problems, including alcohol use disorders to improve service and treatment options for at-risk youth.	NIH continued to support research to evaluate NIAAA's *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide* in emergency department, juvenile justice, school, and primary care settings, and for youth with chronic conditions.

Prevention – SRO-5.15

NIAAA developed a research-based decision tool to help colleges and universities select appropriate strategies to reduce underage and excessive drinking and their consequences.

[19] Fiellin DA. et al. Primary Care–Based Buprenorphine Taper vs Maintenance Therapy for Prescription Opioid Dependence. JAMA Intern Med. 2014;174(12):1947-1954.

The extent of binge drinking and related consequences such as blackouts, assaults and sexual assaults, alcohol poisonings, injuries, and deaths, on college campuses is alarming. Efforts to alter drinking trajectories at this stage have life-changing potential and can significantly reduce the burden of illness resulting from alcohol-related problems. NIAAA-supported research has shown that both individual and environmental approaches to prevention can effectively reduce harmful drinking and its consequences for college students. Working with researchers with expertise in college drinking interventions, NIAAA developed a research-based decision tool to help colleges and universities select appropriate strategies to meet their alcohol intervention goals. The user-friendly decision tool will form the basis of a guide which will allow college presidents and administrators to review the strategies they are currently using as well as explore others that may serve them better. This tool and guide, the NIAAA College Alcohol Interventions Matrix (CollegeAIM), will allow users to search for strategies according to intervention level (e.g., individual, group, campus-wide, community) and evaluate factors such as effectiveness, cost, and ease of implementation. The NIAAA CollegeAIM is being finalized and will be released in 2015. An interactive online version of the decision tool is envisioned.

Treatment – SRO-8.7

Extramural researchers continued to evaluate NIAAA's Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide in emergency department, juvenile justice, school, and primary care settings, and for youth with chronic conditions.

To expand the venues in which at-risk youth can be screened and referred to treatment when appropriate, NIAAA is supporting six five-year studies that are evaluating the youth alcohol screening guide in practice: one in a network of emergency departments, one in a juvenile justice setting, one in a school setting, two in primary care, and one with youth who have a chronic condition (e.g., asthma, diabetes). In addition to evaluating the effectiveness of the screening guide as a predictor of alcohol risk, alcohol use, and related problems, including alcohol use disorder, these studies are also evaluating the effectiveness of the guide as an initial screen for drug use and other behavioral health problems. 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. In FY 2014, NIAAA also continued efforts to increase clinicians' use of the youth alcohol screening guide in primary care and other health care settings by offering an online course developed with Medscape to provide continuing medical education (CME) credits for health care providers. To date, more than 24,000 health care providers have been Medscape certified, and almost 200,000 copies of the youth guide have been distributed.

Research Highlights

<u>Assessing the Impact of Adolescent Alcohol Exposure on the Developing Brain</u>

Adolescence is a period of significant brain maturation and also the time when many individuals initiate and escalate alcohol consumption. Previous studies have shown an association between excessive drinking during adolescence and deficits in brain structure and function; however, it is

not clear whether the deficits predated the onset of alcohol use or occurred as a consequence of it. In 2012, NIAAA launched the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), an ongoing multi-site longitudinal study to address alcohol's effects on normal brain development. The five NCANDA sites have collectively enrolled 800 adolescents ages 12 to 21, and are using advanced brain imaging as well as psychological and behavioral research tools to evaluate brain structure and function, beginning before the participants start to drink. NCANDA's overall objectives are to elucidate the short- and long-term effects of alcohol exposure on the developing brain and to identify the brain characteristics that may predict alcohol use disorder. In a recent study supported through NCANDA, researchers used high resolution magnetic resonance imaging to assess the brain structure of 40 healthy adolescents, ages 12-17, half of whom initiated heavy drinking during a three year follow up. The researchers found that youth who transitioned from no or minimal substance use to heavy drinking had structural abnormalities prior to the initiation of alcohol use. These abnormalities included smaller brain volumes in specific regions of the frontal cortex, an area important for executive functioning. They also showed that youth who transitioned to heavy drinking had significant reductions in brain volumes after alcohol use was initiated, compared to non-drinking youth. These reductions occurred in regions important for sensory integration, feedback processing, motor control, habit learning, visual object recognition, and language comprehension. Whereas both heavy drinking and non-drinking groups showed reductions in brain volumes as a result of normal developmental pruning, those who transitioned to heavy drinking during the study showed accelerated reductions in brain volumes.[20]

Binge drinking during adolescence reduces white matter in specific regions of rat brains with effects that persist into adulthood

Previous studies have demonstrated that heavy binge drinking is associated with reduced white matter integrity in various brain structures, including the corpus callosum, in both adolescents and alcohol dependent adults. In a recent study, researchers used rodent models of adolescent binge drinking and adult alcohol dependence to gain insight into how alcohol affects white matter integrity in the frontal cortex of the brain. They found that adolescent binge drinking reduced the size of anterior branches of the corpus callosum and this neuropathology correlated with higher relapse to drinking in adulthood. The researchers also demonstrated that adolescent binge drinking was associated with damaged myelin, the insulating sheath that forms around the nerve cells that comprise white matter, in the medial prefrontal cortex in adulthood, as well as reduced density of myelin in the medial prefrontal cortex in adolescence. Heavier drinking in adolescence also predicted worse performance on a working memory task in adulthood. These results suggest that adolescent binge drinking may affect white matter integrity in the medial prefrontal cortex through reduction of myelin and these changes may contribute to deficits in executive function in adulthood.[21]

[20] Squeglia LM, Rinker DA, Bartsch H, Castro N, Chung Y, Dale AM, Jernigan TL, Tapert SF. Brain volume reductions in adolescent heavy drinkers. Dev Cogn Neurosci. 2014 Jul;9:117-25. doi: 10.1016/j.dcn.2014.02.005. Epub 2014 Feb 22.

[21] Vargas WM, Bengston L, Gilpin NW, Whitcomb BW, Richardson HN. Alcohol Binge Drinking during Adolescence or Dependence during Adulthood Reduces Prefrontal Myelin in Male Rats. J Neurosci. 2014 Oct 29;34(44):14777-82. doi: 10.1523/JNEUROSCI.3189-13.2014.