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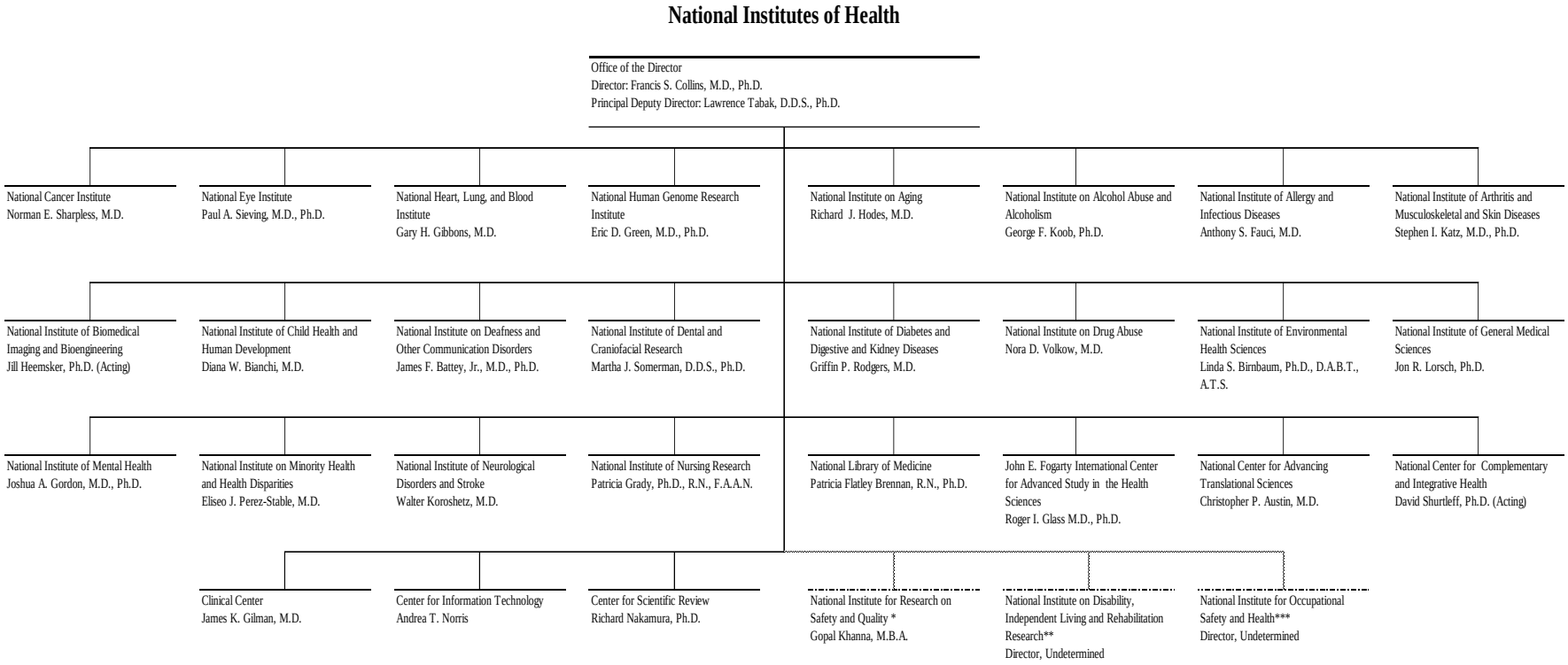
ORGANIZATION CHART



* The FY 2019 Budget proposes to consolidate the Agency for Healthcare Research and Quality into NIH as the National Institute for Research on Safety and Quality

** The FY 2019 Budget proposes to transfer the National Institute on Disability, Independent Living and Rehabilitation Research into NIH from the Administration for Community Living

*** The FY 2019 Budget proposes to transfer the National Institute for Occupational Safety and Health into NIH from the Centers for Disease Control and Prevention

INTRODUCTION AND MISSION

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

As the Nation's biomedical research agency, NIH plays a unique role in turning basic scientific discovery into improved health. Investment by NIH in basic research today lays the foundation for health care breakthroughs in the future. NIH's support of clinical research gives patients new options for treatment and possible cures. The translation of NIH research into treatments and cures depends on a broader ecosystem of stakeholders, including both other federal agencies and private sector companies, and NIH partners with those stakeholders to maximize the impact of its resources. The U.S. biomedical research enterprise depends upon not only NIH's support of cutting edge science and technology but also its investment in nurturing the brightest scientific minds. NIH research also helps drive the economy by creating opportunities for new jobs and new businesses. Through careful stewardship of public resources in pursuit of its mission, NIH aims to enhance the lives of all Americans.

OVERVIEW OF BUDGET REQUEST

Introduction

For FY 2019, NIH requests a total program level of $34.8 billion, which is $0.7 billion above the FY 2018 Annualized Continuing Resolution level.

The Budget supports NIH's mission to seek fundamental knowledge about the nature and behavior of living systems, and applying that knowledge to enhance health, lengthen life, and reduce illness and disability. As a leader of the biomedical research enterprise, NIH leverages public and private resources to tackle major health challenges and take advantage of emerging scientific opportunities to improve diagnosis, prevention, and treatment options for numerous diseases and disorders. Targeted investments in new technology today will push the boundaries of what is possible tomorrow in areas such as imaging, device design, health monitoring, bioinformatics, as well as, countless others. The possibilities for groundbreaking approaches to better human health never have seemed greater, thanks in large part to the rich evidence base of fundamental knowledge of living systems, technological advances, and the ability to integrate and translate vast amounts of information into innovative interventions.

The Budget proposes to begin a long-term effort to provide the necessary funding for stewardship of NIH facilities. NIH owns 281 facilities with over 15 million gross square feet of space, including its research hospital, laboratories, and offices. It has a large and growing backlog of maintenance and repair. At Congressional direction, an independent review is being conducted of the capital needs of the NIH main campus[1]. The Budget increases the B&F account from $128 million to $200 million in order to begin implementing the recommendations of that review, which will be completed by FY 2019.

The President's Budget also proposes the consolidation of targeted HHS research programs within NIH as three new institutes. The Agency for Healthcare Research and Quality (AHRQ) would become the National Institute for Research on Safety and Quality (NIRSQ). The Budget includes $256 million in budget authority for NIRSQ, to preserve key activities to improve the quality and safety of American health care while reducing or eliminating lower priority programs that may potentially overlap with activities administered by other components of HHS. In addition, NIRSQ is projected to receive $124 million in mandatory resources from the Patient-Centered Outcomes Research Trust Fund. The National Institute for Occupational Safety and Health, would move to NIH from the Centers for Disease Control and Prevention with $255 million in budget authority, including $55 million in mandatory resources for the Energy Employees Occupational Illness Compensation Program. The National Institute on Disability, Independent Living, and Rehabilitation Research would move to NIH from the Administration for Community Living, with $95 million in budget authority.

In FY 2017, Congress enacted the 21st Century Cures Act, authorizing $4.8 billion over ten years in support of high priority NIH initiatives and research areas: 1) the Precision Medicine Initiative's All of Us Research Program, 2) the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, 3) the Beau Biden Cancer Moonshot, and 4) Regenerative Medicine. The FY 2019 Budget includes the full $711 million authorized for

[1] House Report 115-244.

these initiatives. The funding for the Cancer Moonshot ($400 million) is to be transferred to the National Cancer Institute; and the funding for the BRAIN Initiative is to be transferred to the National Institute of Neurological Disorders and Stroke ($57.5 million) and the National Institute of Mental Health ($57.5 million).

NIH's FY 2019 research investments will be guided by the NIH-Wide Strategic Plan for FY 2016-2020.[2] Some of the strategies the Plan identified as highest priority for FY 2019 are summarized in the following themes:

1. Tackling Complex Challenges by Leveraging Partnerships
   NIH is exploring ways of partnering that leverage both public and private resources to tackle major public health issues, create efficiencies of scale, and assure careful stewardship of public funds. Through its partnerships, NIH will collaborate across the government and with private partners to ensure strategic investments, reduce redundancies, and hasten the translation of research into practice.

2. Supporting Basic Research to Drive New Understanding of Health and Disease
   Basic research is the foundation for all progress in biomedical research. NIH plans to invest in new and ongoing initiatives to learn more about how biological systems function, and to develop tools to study these systems, from the behavior of whole organisms down to the individual cell and its components.

3. Investing in Translational and Clinical Research to Improve Health
   For a discovery to move from the lab into practice, fundamental scientific knowledge must undergo a rigorous translational and clinical research agenda that will test and optimize potential health interventions and approaches based upon it. Increasingly, NIH is investing in translational and clinical research designed to provide all patients with interventions tuned to their individual characteristics.

4. Fostering an Inclusive and Talented Biomedical Research Workforce for Today and Tomorrow
   NIH will invest in recruiting and retaining a robust, talented research workforce to sustain our progress and spur future innovation. Focusing on early and mid-career stages will ensure the vitality of the next generation of researchers.

By using these themes to guide strategic investments, NIH hopes to significantly advance its mission towards improving the health of all Americans.

Theme 1: Tackling Complex Challenges by Leveraging Partnerships

Translating NIH's basic research findings into treatments and cures requires efficient collaborations within NIH as well as with other government, academic, industry, and non-profit partners. NIH works closely with federal partners to streamline processes, collaborate on research projects, and share the agency's evidence base to catalyze efforts across the government

[2] https://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2016-2020-508.pdf

to improve health for all Americans. Partnerships also enable the public and private sectors to work synergistically toward medical advances, accomplishing goals that cannot readily be achieved by acting alone. Leveraging resources and expertise, NIH is engaged in several significant partnerships addressing issues from Alzheimer's disease to cancer biomarkers to the opioid crisis (see box under Theme 3 below). Continued emphasis on public-private partnerships will ensure NIH's careful stewardship of public funds and increase the pace of research to benefit patients more quickly.

Accelerating Medicines Partnership

One of NIH's most successful partnership models is the Accelerating Medicines Partnership (AMP), a public-private partnership between NIH, the Food and Drug Administration (FDA), 10 biopharmaceutical companies, and multiple non-profit organizations. Managed by the Foundation for NIH (FNIH), AMP aims to transform the current model for developing new diagnostics and treatments by jointly identifying and validating promising biological targets for therapeutics. Ultimately, the goal is to increase the number of new diagnostics and therapies for patients and to reduce the time and cost of developing them. AMP was launched in 2014 with three projects: Alzheimer's disease (AD), type 2 diabetes (T2D), and the autoimmune disorders rheumatoid arthritis and systemic lupus erythematosus (RA/Lupus). An additional partnership on Parkinson's disease has just been initiated. A critical component of the partnership is that all partners are making the AMP data publicly accessible for further analysis by the broader biomedical community. Each project has already made significant contributions: AMP-AD has provided the field with tools and data to significantly enhance understanding of how AD alters the brain; the T2D Knowledge Portal now makes available genetic and clinical data sets covering many ethnicities, as well as European data, for diabetes research; and the RA/lupus project released data in the fall of 2017 derived from new methods to isolate and analyze individual cells important to understanding autoimmune diseases. Based on the successes of these projects and partner interest, AMP anticipates launching a fourth project in early 2018 focusing on Parkinson's disease (PD). Collectively, the AMP projects allow research, regulatory, and industry ideas and personnel to work together to increase the number and effectiveness of targeted therapies.

Partnerships for Accelerating Cancer Therapies

Capitalizing on the scientific opportunities presented by the Beau Biden Cancer Moonshot, NIH is building partnerships to spur the development of new cancer therapeutics. Cancer immunotherapy, which bolsters the immune system's natural capacity to attack cancer cells, have yielded dramatic, positive results for many patients with several types of cancer. These approaches do not work for all cancer patients, however, and better understanding the mechanisms by which these treatments and others work or do not work in patients will improve patient outcomes. For instance, the identification of biomarkers, molecular indicators of disease, could be used to predict how a patient will respond to a particular treatment. Joining forces to build a better evidence-base to understand cancer treatment, NIH, the FDA, and 11 biopharmaceutical companies formed the Partnership for Accelerating Cancer Therapies (PACT) in October 2017. This 5-year, $215 million public-private partnership aims to bring cancer therapies to patients in less time. Managed by the Foundation for NIH, PACT initially will focus

on developing and standardizing new biomarkers to predict response to cancer therapy. Once developed and validated, such biomarkers may be used to enable faster regulatory approval. Furthermore, the partnership will provide the research community with a widely available database for PACT research and other data. This cross-sector collaborative effort will enable shared expertise and resources to advance science for the maximum benefit of patients.

Also in support of the Cancer Moonshot, in January 2017, the National Cancer Institute (NCI) launched the NCI Formulary, a public-private partnership between NCI and pharmaceutical and biotechnology companies. By working with the NCI Formulary, investigators eliminate the need to negotiate directly with companies, thus expediting the start of clinical trials by up to 18 months and facilitating faster development of new therapies for patients. Since its launch, the NCI Formulary has nearly doubled the number of agents it offers, providing researchers with access to a total of 27 targeted agents through partnerships with nine companies as of December 2017. As the ability to target the selection of cancer therapies to individual characteristics grows, the NCI Formulary's role in enabling investigators to conduct combination studies with multiple agents from different companies will become even more vital.

National Collaborative on Childhood Obesity Research

Collaborating with other federal agencies to address an expanding public health need, NIH plays an active role in the National Collaborative on Childhood Obesity Research (NCCOR). Obesity during childhood can lead to numerous negative physical and psychological effects including high blood pressure, breathing problems, musculoskeletal discomfort, depression, and low self-esteem, among others.[3] This problem is growing; approximately one in five school-aged children in the U.S. are obese, which is more than three times greater than the percentage of children who were obese in the 1970s.[4] To address this issue, NIH joined the Centers for Disease Control and Prevention (CDC), U.S. Department of Agriculture, and the Robert Wood Johnson Foundation to form NCCOR in 2009. NCCOR's focus is on evaluating and identifying effective interventions (particularly policy and environmental interventions) at the individual, community, and population levels in the areas of nutrition, physical activity, and weight control with a special emphasis on the lower-income and racial/ethnic populations at highest risk. From late 2017 through 2020, NCCOR will focus on efforts to accelerate progress against childhood obesity through better and more consistent measurement, including better tools and practices for measuring food intake and physical activity. Better measures will allow for further standardization, meta-analysis, and synthesis within the childhood obesity research field.

Innovation through Competition

Another type of partnership that NIH plans to expand is the use of prize competitions to complement traditional forms of financial support for the nation's biomedical researchers (i.e. grants, contracts, etc.). The Budget allocates $50 million for prize competitions under the authority of Section 105 of the America COMPETES Reauthorization Act of 2010. This will focus on the types of innovation highlighted in Section 2002 of the 21st Century Cures Act, including monitoring the effect of innovations funded through prize competitions on advancing

[3] https://www.cdc.gov/obesity/childhood/causes.html
[4] https://www.cdc.gov/healthyschools/obesity/facts.htm

biomedical science or improving health outcomes. The prize funding will be housed in the Common Fund and available for competitions sponsored by any NIH Institute, Center, or Office.

Theme 2: Supporting Basic Research to Drive New Understanding of Health and Disease

NIH is the largest single funder of basic biomedical research in the U.S, providing a critical research foundation for both the public and private sectors to build upon. NIH supports a robust basic research portfolio which studies both how healthy living systems function outside the context of a particular disease as well as research to understand the mechanisms of disease. Studies of healthy systems help researchers recognize how such systems go wrong in cases of disease and injury, and which elements might need to be restored in order to treat such conditions. Characterizing the underlying mechanisms of disease enables scientists to comprehend the causes of disease onset and progression, identify key risk factors, or scout out new potential targets for therapies and cures.

It is difficult to predict where dramatic new scientific breakthroughs will arise, given that many involve unexpected connections among otherwise incremental advances. In order to maintain the flexibility to capture unanticipated breakthroughs as well as making steady progress in as many research areas as possible, NIH funds a broad spectrum of basic science research. In addition, NIH provides the resources, infrastructure, and overarching vision that allows the field to capitalize on scientific opportunities as they arise.

Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative

The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is a key example of NIH's approach to fostering basic research. The BRAIN initiative aims to revolutionize our understanding of the human brain by supporting the development and application of innovative technologies that allow researchers to study how individual cells and complex neural circuits interact in both time and space. By catalyzing the development of new research technologies, the BRAIN initiative supports advancements that will allow scientists across disciplines, not just those funded by the initiative, to push the frontiers of their research, from manipulating and monitoring neural activity at unprecedented scales to understanding the molecular "census" of the cells in the brain well enough to manipulate highly specific populations. For example, one project looked at improving mathematical methods for analyzing human brain activity from functional magnetic resonance imaging (fMRI) scans to better understand the underlying networks of neural connections within the brain. These improved methods allowed researchers to look at how those underlying networks are changed in patients with an early stage of dementia called mild cognitive impairment, which one day may allow for earlier diagnosis of the disease. In FY 2019, NIH will support research projects to advance progress toward the goals outlined in *BRAIN 2025: A Scientific Vision*[5].

Transformative High-Resolution Cryo-Electron Microscopy (Cryo-EM) Program

The NIH Common Fund supports transformative, trans-NIH research that capitalizes on scientific opportunities, often with the goal of advancing basic research. The Transformative

[5] https://www.braininitiative.nih.gov/pdf/BRAIN2025_508C.pdf

High-Resolution Cryo-Electron Microscopy (Cryo-EM) program is one example of how the Common Fund drives basic research. [6] Cryo-EM, named Nature Methods' "Method of the Year" in 2016, is a technique used to image frozen biological molecules without the use of structure-altering dyes or fixatives, providing a more accurate picture of the molecules and greater understanding of biological function. An accurate, high-resolution understanding of the structure of biological molecules can provide essential information about how molecules function, and can reveal potential targets for therapies in disease. For example, cryo-EM has been used to create a detailed structure of the protein CFTR, which is mutated in patients with cystic fibrosis, allowing researchers to better understand how the protein's function is disrupted, and how it might be rescued. This Common Fund program aims to provide nationwide access for researchers to cryo-EM through the creation of national service centers, improvement of the technology, and the development of an expert workforce, broadening access to transformative tools for researchers across the country.

Human BioMolecular Atlas Program (HuBMAP)

Another NIH Common Fund program supporting basic research is the Human BioMolecular Atlas Program (HuBMAP). Humans are made up of diverse cell types formed during the course of development, each with unique functions and roles that contribute to physiological structures and processes within the body. The organization and variability of these cells have a profound impact on the function of different tissues, the process of aging, and the emergence of diseases and conditions. New technologies are allowing researchers to explore molecular differences and characterize new types of cells down to the individual cellular level. HuBMAP supports technology development and research to take a census of cell types in human tissues, to understand the relationships between cellular organization and function, and to understand how much individual cells vary within a particular cell type. By generating a detailed molecular "atlas" of cell types within the human body, basic researchers will provide data that can be used to better understand disease states and develop new, targeted therapies.

Exploring the Frontiers of Gene Editing

Gene editing techniques to precisely change specific sequences in the human genome raises the possibility of a fundamentally new approach to treat diseases, such as genetically engineered immune cells to fight cancer (immunotherapy) or use of the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) method to "fix" the mutations that cause sickle cell disease. However, efficacy, specificity, and delivery of modified cells remain challenging. The NIH Common Fund is launching a new program called "Somatic Cell Genome Editing" in FY 2018 to improve the efficacy and specificity of genome editing approaches. The research tools developed through this program will be made widely available to the research community to reduce the time and cost required to develop new therapies.

NIH believes that these programs, and others like them, represent a crucial investment in the early stages of biomedical research, providing essential information on how living systems work. By making a substantial investment in basic research, NIH fulfills its role as the foundation of

[6] https://commonfund.nih.gov/CryoEM

the biomedical research enterprise, feeding discoveries into the system that will ultimately lead to interventions, treatments, and cures.

Theme 3: Investing in Translational and Clinical Research to Improve Health

Building on a robust foundation of basic research, NIH supports translational research that applies fundamental knowledge to discover new strategies for intervening in disease processes through better detection, prevention, or treatment. These strategies, which could develop a potential medication, a new vaccine, a medical device, a community-based prevention program, or a wide range of other intervention types, are then optimized and tested in clinical or real world settings to assess their efficacy and effectiveness. NIH is deliberate in its support of translational and clinical sciences, following the guidance of its strategic plan to fund those studies in which the scientific opportunities are ripe, and the public health needs, whether emerging or chronic, are greatest. As with basic research, NIH not only supports translational and clinical studies directly, but also supports the creation of the infrastructure, resources, and tools to provide a platform for innovation. To facilitate integrated understanding of health and disease at all levels, from molecular underpinnings to social factors to treatment response, NIH is investing in large population studies to learn more about how we are the same and how we are different. This integration will allow for unprecedented precision in the ways in which health is addressed, making it possible for every individual to receive preventive and therapeutic care tailored specifically to their needs, ushering in an era of precision medicine.

Regenerative Medicine

Fundamental understanding of development, cellular and organ functioning, and other factors have given rise to the promising multidisciplinary field of regenerative medicine, which seeks to develop functional tissues and organs to repair or replace biological structure and function that has been lost due to injury, disease, or aging. These aims are achieved by integrating tissue engineering and cell-based therapy techniques. For example, NIH supports the (Re)Building a Kidney Consortium, whose goal is to coordinate and support studies that will result in the ability to replicate or repair kidney function. The Consortium supports a variety of translational research approaches, including bioengineering, 3D printing, and developing novel in vitro models to study organ structure and function.

Preclinical studies have demonstrated that regenerative medicine approaches may be effective, and some clinical trials on the safety and efficacy of these therapies are underway. Given the potential promise of regenerative medicine therapies, the 21st Century Cures Act (P.L.114-255) included a Regenerative Medicine Innovation project, providing $30 million over 4 years for clinical research with adult stem cells. In September 2017, NIH issued the first awards under this project, funding eight clinical research projects to advance understanding of and discover new treatments for common diseases such as diabetes, anemia, eye diseases, and chronic skin ulcers, as well as rare diseases such as idiopathic pulmonary fibrosis, sickle cell disease, and inherited skin diseases. These awards were made in coordination with FDA, which will facilitate a smoother regulatory approval process as therapies are developed. The FY 2019 request includes $10 million in Innovation Funds for this area of research, which will be augmented by matching funds and individual IC support.

Universal Influenza Vaccine

The flu (influenza) virus remains a deadly and costly pathogen, placing a substantial health and economic burden on the U.S. and across the world each year. In the U.S., CDC estimates that the flu has resulted in between 9.2 million and 35.6 million illnesses, between 140,000 and 710,000 hospitalizations, and between 12,000 and 56,000 deaths annually since 2010,[7] all of which results in an estimated $27 billion in health costs alone.[8] Vaccination is the most effective way to reduce flu morbidity and mortality. Annual seasonal flu vaccines confer protection against some, but not all, flu strains and must be developed months in advance of the flu season. This strategy relies heavily on scientists being able to predict ahead of time which strains will be in circulation each year. The result is that a vaccine may be less effective if a strain not included in vaccine development predominates—a particular concern in the case of rare but unpredictable pandemic outbreaks. This underscores the need for new approaches to flu vaccine R&D, in particular, the development of a single "universal flu vaccine" that would provide safe, effective and long-lasting immunity against a broad spectrum of flu viruses, both seasonal and novel. NIH-funded researchers are making progress toward this goal by targeting a particular protein on the surface of the flu virus, several versions of which are being evaluated for further clinical study. In addition, clinical trials already are underway for an alternative approach involving a DNA-based vaccine and a seasonal booster. Continued investment in this research will enable the fastest possible vaccine development to protect millions of people from infection.

Addressing Zika Virus Infection

Threats to public health evolve as new disease-causing pathogens emerge or familiar ones reemerge with new properties, and NIH is at the forefront of defending against these threats. In 2015, the threat from the Zika virus rose as infection spread rapidly across Central and South America. The Zika virus is primarily transmitted to humans through mosquitoes, and for most people symptoms generally are mild. However, transmission from an infected pregnant woman to her baby can result in serious birth defects, including microcephaly; a concern which has grown since the first case of locally transmitted Zika virus in the continental United States was confirmed in July 2016. To address this problem, NIH is working with government, academic, and industry partners to accelerate research to understand how the Zika virus causes disease, as well as to develop treatments and vaccines. Currently underway are two population studies: the first to understand the effect of Zika infection on pregnant women and babies, and the second to gain insight on outcomes of infection acquired after birth in babies and children.

In addition, mouse models have been used to help NIH and their partners to develop vaccine candidates to restrict Zika virus transmission from mother to fetus in pregnant mice. Mouse models also have shown that Hydroxychloroquine, a drug approved by the FDA to treat malaria and certain autoimmune diseases in pregnant women, appears to reduce transmission of Zika virus from pregnant mice to their fetuses. Through the NIH drug repurposing screening program, two further classes of compounds have been identified that might be effective against Zika. As translational research bears fruit, NIH is now beginning to launch clinical trials in humans. In 2017, NIH launched an efficacy trial on an experimental DNA vaccine against Zika

[7] https://www.cdc.gov/flu/about/disease/burden.htm.
[8] https://www.niaid.nih.gov/sites/default/files/univflu508b.pdf.

in the U.S. and Central and South America. Early reports from Phase I clinical trials show that the vaccine is safe and induces an immune response in healthy humans.[9]

Tissue Chip for Drug Screening Program

Translating how a basic finding from the laboratory might work in the human body is a challenging process. NIH supports a number of initiatives and projects to develop new tools and resources to overcome these challenges and hasten progress. One such initiative, the Tissue Chip for Drug Screening program, is designed to facilitate faster development of new therapeutics by creating novel model systems to screen potential new drugs that more accurately mimic the human body than current models. Conducted in collaboration with the Defense Advanced Research Projects Agency (DARPA), and the FDA, the program aims to develop microfabricated chips—called "tissue chips" or "organs-on-chips"— capable of maintaining living human cells and tissues. These cells and tissues are organized to model intact human organ systems, with the goal of eventually creating an integrated human-body-on-a-chip. Once developed and integrated, researchers can use these models to predict whether a candidate drug, vaccine, or biologic agent is safe or toxic in humans in a faster and more effective way than current methods. For example, a team of scientists have created EVATAR™, a miniature working 3-D representation of the female reproductive tract, along with the liver.[10] Tissue chips may be used to study both normal function and disease states. In September 2017, NIH announced 13 new awards to study a wide range of common and rare diseases.[11] In the second phase of these awards, researchers will partner with pharmaceutical companies to evaluate the usefulness of these models in assessing the effectiveness of candidate drugs.

All of Us Research Program

Far too many diseases do not have a proven means of prevention or effective treatment, and in particular, what works for one person may not always work for another. Precision medicine is a revolutionary approach for disease prevention and treatment that takes into account individual differences in lifestyle, environment, and biology, such as genetics. The first step in this approach is to provide a window into these different factors to understand their respective and combined influences on both health and disease. This understanding would enable the development of interventions tailored towards individuals for optimal success and efficiency. Spearheading this approach, the *All of Us* Research Program, launched in FY 2016, is an ambitious effort to gather data over many years from one million or more people living in the United States. Unlike research studies that are focused on a specific disease or population, *All of Us* will serve as a national research resource to inform thousands of studies, covering a wide variety of health conditions. At the same time, participants may be able to learn more about their own health and contribute to an effort that may advance the health of generations to come.

[9] Gaudinski, M.R., et al. *Lancet* 2017;S0140-6736(17)33105-7. PMID: 29217376.
[10] Xiao S, et al. A microfluidic culture model of the human reproductive tract and 28-day menstrual cycle. *Nat Commun* 2017;8:14584. PMID: 28350383
[11] https://www.nih.gov/news-events/news-releases/nih-awards-15-million-support-development-3-d-human-tissue-models

The *All of Us* Research Program collaborates with other federal agencies within HHS and across the government, including the FDA, the Office of the National Coordinator for Health Information Technology (ONC), the Office for Civil Rights (OCR), the Department of Veterans Affairs (VA), the Department of Defense (DoD), and the Department of Energy (DoE). Indicative of the importance of this initiative, the 21st Century Cures Act included nearly $1.5 billion for *All of Us* over the next decade, and several key implementation milestones already have been reached. In May 2017, participant enrollment began at select sites. This first wave of beta testers is helping to identify and fix problems with the system before full enrollment is launched in the spring of 2018. NIH also has invested in a state-of-the-art biobank and built big data IT systems to transfer and store data for use by researchers, with safeguards in place to keep participants' information private and secure. In July 2017, NIH announced its first four community partner awards, totaling $1.7 million, to begin building a national network of trusted leaders to motivate diverse communities to join the *All of Us* Research Program. Shortly after, NIH announced fourteen national community groups and health care provider association awards, totaling $1 million, to help raise awareness about the program by educating communities about the benefits of participation in this landmark program. NIH has also established a partnership with the National Network of Libraries of Medicine, totaling $4.5 million, to support community engagement efforts by public libraries across the nation and improve participant access. Representing a new era of treatment and disease prevention, continued support of this groundbreaking effort will accelerate research and improve health.

Environmental Influences on Child Health Outcomes (ECHO) Program

NIH is supporting another cohort study to better understand the impact of the environment on health. In FY 2016, NIH launched the Environmental Influences on Child Health Outcomes (ECHO) program to investigate the effect of a broad range of exposures—from air pollution and chemicals in our neighborhoods, to societal factors such as stress, to individual behaviors like sleep and diet—during the sensitive developmental window from conception through early childhood. In addition to leveraging existing cohorts, another critical component of ECHO is leveraging the NIH-funded Institutional Development Awards (IDeA) program to build state-of-the art pediatric clinical research networks in rural and medically underserved areas so that children from these communities can more easily participate in clinical trials. ECHO studies will focus on key pediatric outcomes that have a high public health impact, including upper and lower airway health and development, obesity, brain development, and positive health. With $157 million in awards announced in FY 2016 to build infrastructure and capacity, the ECHO program is off to a promising start. In FY 2017, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the IDeA States Clinical Trials Network are collaborating to support the Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW) study. ACT NOW will fund research on opioids and pregnancy outcomes by addressing critical gaps on how best to treat and manage opioid withdrawal syndrome in newborns. Every baby should have the best opportunity to remain healthy and thrive throughout childhood; ECHO answers this call, helping us understand with better precision the factors that contribute to optimal health in children.

Advances in Cancer Treatment

Cancer remains a leading cause of death in the U.S. and around the world. Complicating matters is the fact that cancer is not a single disease, but is a complex of more than 100 diseases in which genetic changes disrupt cell function. Given the complicated nature of cancer, it is essential to harness new technologies and approaches to treat this often deadly condition. Leveraging new knowledge of the precise factors that influence disease, NIH is pioneering the use of precision medicine in treatment approaches to better target the right treatments to the right people. For example, in FY 2015, the National Cancer Institute (NCI) launched Molecular Analysis for Therapy Choice (NCI-MATCH), a unique precision medicine Phase 2 clinical trial, to determine whether targeted therapies for people whose tumors have specific gene mutations will be effective regardless of their cancer type. Building on this approach, in July 2017, enrollment began for Pediatric MATCH. Similar to MATCH, this nationwide Phase 2 trial will explore whether targeted therapies can be effective for children and adolescents with cancer tumors that have specific genetic signatures and have progressed during or after standard therapy. Precision medicine trials like MATCH have the potential to accelerate progress in identifying more effective treatments for people with cancer, and these clinical trials illuminate the way for future endeavors.

Cancer immunotherapy is another rapidly advancing approach to cancer treatment. Patients with a variety of cancers, including melanoma, non-small cell lung cancer, leukemia, colorectal cancer, and breast cancer have already benefitted from immunotherapy, and NIH-supported researchers hope to expand these results to other disease areas. Two major advances in this area include Keytruda, the first immunotherapy to be FDA-approved for all cancers with a specific biomarker, regardless of where the cancer is found in the body,[12] and chimeric antigen receptor T-cells (CAR-T), a treatment that uses a patient's own immune cells to more effectively combat cancer.[13] To harmonize research efforts in this area, the Cancer Moonshot Blue Ribbon Panel established the Cancer Immunology Working Group. This working group will create and implement a national strategy to discover and evaluate novel immunotherapies that, in the short term, increase the cure rate in cancer patients and eventually provide the opportunity to develop immune-based approaches that prevent cancers of all types.[14] Furthermore, NIH-supported researchers are also combining precision medicine and cancer immunotherapy approaches to understand how some cancers become resistant to cancer immunotherapy.[15] Cancer immunotherapy alone, or in combination with other treatments such as chemotherapy, has the potential to more effectively treat patients with many types of cancer.

[12] https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm560167.htm
[13] https://directorsblog.nih.gov/2017/08/30/fda-approves-first-car-t-cell-therapy-for-pediatric-acute-lymphoblastic-leukemia/
[14] https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel/cancer-immunology-working-group-report.pdf
[15] https://projectreporter.nih.gov/project_info_description.cfm?aid=9087003&icde=32574780

Combatting the Opioid Epidemic

Opioid misuse and addiction is an ongoing and rapidly evolving public health crisis. According to the Centers for Disease Control and Prevention (CDC), in 2016 alone more than 42,000 deaths involved opioid use. Driven by the abuse and misuse of prescription pain relievers such as oxycodone, synthetic opioids such as fentanyl, and the illegal drug heroin, the opioid epidemic not only poses a tremendous public health challenge, but also threatens our social and economic welfare. The urgency and scale of this crisis calls for innovative scientific solutions.

As part of a larger government-wide effort to address the opioid crisis, NIH will enhance existing research efforts, investing $850 million (including $750 million from an HHS-wide $10 billion investment) in an ambitious series of projects, including a multi-year public-private partnership to accelerate the development of safe, non-addictive, and effective strategies to prevent and treat pain, opioid misuse, and overdose and to help optimize their implementation. In consultation with experts from government, industry, and academia, NIH has proposed a coordinated strategy with two primary aims: 1. Develop new formulations and combinations of medications to treat opioid use disorders and prevent and reverse overdose; and 2. Accelerate development of new non-addictive pain therapies.

Several effective therapies exist to treat opioid use disorder and reverse overdose from opioid drugs. Medication-assisted treatment in which patients with opioid use disorder receive medications (methadone, buprenorphine, or naloxone) in conjunction with psychosocial support, is effective. However, only a small proportion of patients are retained in treatment for long-term recovery. NIH will increase significantly its research investment in treatments for substance use disorders, and work with private-sector partners to develop new formulations and combinations of medications to treat opioid use disorders and prevent and reverse overdose, with the goal of making a wide range of therapeutic options accessible to those who need them as quickly as possible.

Much of the opioid epidemic has struck patients seeking relief from very real sources of pain. The development of new pain treatments that lack the addictive properties of many of today's pain medications could prevent many patients from developing opioid use disorder. NIH will work with the Food and Drug Administration and pharmaceutical partners to build a public-private partnership to accelerate the development of new non-addictive pain therapies and make these widely available to patients in need.

Finally, NIH will work with other federal partners to incentivize development of new therapies and to develop and evaluate metrics for high-quality treatment.

Theme 4: Fostering an Inclusive and Talented Biomedical Research Workforce for Today and Tomorrow

A sustainable and inclusive biomedical research workforce, comprising all levels of researchers, is necessary for ensuring innovation in the biomedical and behavioral sciences. For NIH to achieve its mission, inquisitive and talented people such as established scientists, postdoctoral researchers, students, and clinicians are essential. NIH remains committed to the development, support, and retention of a motivated workforce that includes varied backgrounds and experiences as well as a broad range of expertise. NIH cultivates the human capital needed to fulfill its mission by investing in outstanding researchers with high potential, strengthening an inclusive biomedical research community, and by investing in clinician-scientists.

Supporting Early-Stage and Mid-Career Investigators

Attracting and retaining creative individuals in the biomedical research workforce requires a stable environment and opportunities for career growth. At a time where the number of applications received by NIH has risen at a rate faster than that of its budget, the biomedical workforce has grown increasingly concerned about the long-term stability of the biomedical research enterprise. In what has become an increasingly hypercompetitive environment, an investigator must spend more time seeking funds and consequently less time conducting science. This is especially challenging to those just starting their career and to recently-established independent investigators who, faced by the prospect of struggling for funding, may turn away from a career in science. This disincentive threatens the future of biomedical research.

To help create a stable path for the next generation workforce and ensure the best and brightest scientists remain in research, NIH launched the Next Generation Researchers Initiative (NGRI) in August 2017.[16] The 21st Century Cures Act encouraged NIH to develop policies that will promote earlier independence and increased rates of funding for early career investigators through the creation of the NGRI, which seeks to address challenges faced by researchers trying to embark upon and sustain independent research careers. To achieve this aim, all NIH Institutes and Centers (ICs) are committing to prioritize awards that will fund promising investigators at early stages in their career, including those seeking their first independent substantive research award. For FY 2019, the Budget includes a dedicated fund of $100 million in the Office of the Director that Institutes and Centers would be able to draw on to supplement the NGRI efforts undertaken with their own appropriations.

As part of NGRI, each IC will develop evidence-based strategies to support their mission-specific workforce that consider factors such as emerging areas of scientific inquiry, the distribution of the scientific portfolio, and the projected needs of the scientific workforce. New methods for measuring the effects of these strategies will be devised, with special attention paid to assessing the ability to enhance workforce inclusion. Using these strategies, NIH will be able to monitor closely its success in ensuring that talented early career investigators have improved opportunities to launch and sustain a successful career.

Supporting Outstanding Scientists

Another strategy to improve stability for promising scientists is to provide steady support for a longer period of time and with greater flexibility to pursue promising scientific directions. To this end, several NIH ICs have implemented new funding opportunities to support an investigator's entire program of research, rather than an individual project, so that researchers can pursue unexpected avenues of inquiry as they arise. One such award, through the National Institute of General Medical Sciences (NIGMS), is the Maximizing Investigators' Research Award (MIRA).[17] The initial pilot program for MIRA included separate funding opportunities for both established investigators and early-stage investigators. Following successful completion of the pilot, NIGMS elected to expand the eligibility criteria of the program in order to provide

[16] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-101.html
[17] https://www.nigms.nih.gov/Research/mechanisms/MIRA/Pages/default.aspx

additional participatory opportunities for investigators. A strategy for hastening the pathway to a successful scientific career of especially promising early investigators is funded through the Common Fund's High-Risk, High-Reward Research program.[18] In FY 2017, NIH issued 86 awards for this program.[19] The Early Independence Award supports outstanding junior scientists with the intellect, scientific creativity, drive, and maturity to flourish independently by bypassing the traditional post-doctoral training period. [20] Receiving this award accelerates the entry of exceptional junior investigators into positions of independent research. Additionally, the New Innovator award supports exceptionally creative early career investigators who propose innovative, high impact projects.[21] To be eligible for this award, a researcher must be within 10 years of completing a doctoral degree or medical residency and have never received an NIH Research Project Grant or equivalent award.

Strengthening the Inclusiveness of the Workforce

Technological advances and a new understanding of the vast complexity of biological systems and their behaviors are driving biomedical research toward increasingly multidisciplinary work. Career paths outside of academia also have become increasingly common and important in sustaining a robust biomedical research enterprise. Given the changing research environment, it is vital to equip early-stage scientists with a range of skills and experiences as well as to ensure a workforce that represents the racial, cultural, demographic, and geographic richness embodied by our country.

NIH strives for a biomedical workforce that reflects the range of backgrounds of the public it serves. To foster this value, NIH's National Research Mentoring Network (NRMN)[22] was created to increase access to high-quality research mentorship and networking opportunities for individuals with disparate backgrounds by establishing a nationwide, interconnected set of skilled mentors linked to mentees from a variety of scientific disciplines. In addition to establishing mentor-mentee relationships, the program seeks to develop best practices for mentoring, provide training for mentors, as well as professional opportunities for mentees. A trio of awards and initiatives serve as premiere examples of the programs NIH designs in order to encourage individuals with varied backgrounds to participate in science. Now in its third year, the Building Infrastructure Leading to Diversity (BUILD) Initiative supports training awards designed to apply experimental approaches towards attracting and retaining an inclusive array of students into the training pipeline. BUILD awardees work with multiple partnering institutions with high concentrations of students from disadvantaged backgrounds to test and implement transformative, broad-based approaches to the training and mentoring of students to undertake biomedical research.[23] Another program, the Institutional Research and Academic Career Development Awards (IRACDA),[24] promotes consortia between research-intensive institutions and partner institutions that have a historical mission of and a demonstrated commitment to providing training, encouragement, and assistance to students from underrepresented groups.

[18] https://commonfund.nih.gov/earlyindependence
[19] https://www.nih.gov/news-events/news-releases/nih-directors-high-risk-research-awards-announced-2017
[20] https://commonfund.nih.gov/earlyindependence
[21] https://commonfund.nih.gov/newinnovator
[22] https://www.nigms.nih.gov/training/dpc/pages/nrmn.aspx
[23] https://www.nigms.nih.gov/training/dpc/pages/build.aspx
[24] https://www.nigms.nih.gov/Training/CareerDev/Pages/TWDInstRes.aspx

Similarly, the Research Initiative for Scientific Enhancement (RISE) program[25] provides support to institutions with a commitment and history of developing students from populations underrepresented in biomedical sciences.

Supporting clinician-scientists

One of the most important functions of the NIH is to foster the translation of basic biomedical research findings from the laboratory bench to the patients and communities that can benefit from advances in medicine. By recruiting and supporting clinician-scientists in the biomedical research workforce the NIH is able to both build a clinical perspective into research activities and encourage practitioners to consider the research implications of their observations and practices. Recruiting clinicians into research, however, can be challenging. The training required to be both a practicing physician, nurse, or other clinician coupled with the lengthy requirements of research degrees can discourage candidates. Based on the recommendations from three workshops held in 2016, NIH recently released a Funding Opportunity Announcement entitled Stimulating Access to Research in Residency (StARR) to provide support for institutional research in residency programs.[26] Also, NIH issued a Request for Information (RFI) to gather input on potential revisions to the Medical Scientists Training Program (MSTP), which trains students pursuing dual health profession and Ph.D. degrees. This input will be reflected in a new Funding Opportunity Announcement to be released in FY 2018. Through these and other efforts, NIH is looking to both improve the quality of clinician-researcher training and to shorten the time each individual needs to invest in training.

Advancing Data Science

In 2012, NIH established the Big Data to Knowledge (BD2K) initiative and created a new Associate Director for Data Science (ADDS) position. In the years since, NIH has established extramural Centers of Excellence, piloted a "Data Commons," and supported enhanced training of data scientists and bioinformaticians. In FY 2019, NIH would begin the next phase of its data science activities with a $30 million fund, managed by the ADDS, to build on the success of BD2K as that initiative enters its final stages.

Optimize NIH

The Optimize NIH Initiative, part of the HHS effort to implement OMB Memorandum M-17-22 (Comprehensive Plan for Reforming the Federal Government and Reducing the Federal Civilian Workforce), is intended to increase the efficiency and effectiveness of the administrative operations that advance our scientific mission. The goals of the Initiative are improving services through coordinating and optimizing comparable functions across selected functional areas, maximizing employee engagement, and enhancing stewardship of taxpayer dollars. The Initiative will consist of three phases:

[25] https://www.nigms.nih.gov/Training/RISE/Pages/default.aspx
[26] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-101.html

1. Enterprise-wide functional cores
2. Harmonization of scientific or mission-specific functions
3. Operational service center cores

For each phase, NIH will approach this optimization effort in a data-driven, scientific manner. NIH staff will perform a review to identify, map, and analyze all the key processes within the functions and identify opportunities for improvement. After this detailed process review, an implementation plan will be developed. Information technology needs and staffing gaps or redundancies will be evaluated, and lessons learned from each phase will be applied to the other phases. We anticipate that the re-engineering of our processes will yield the single largest increase in our overall efficiency.

Initially, the Optimize NIH Initiative will focus on enterprise-wide functional cores in the following three areas: Ethics, FOIA, and Committee Management. This phase is under way, and NIH anticipates that additional enterprise-wide functional cores may be reviewed for future optimization opportunities. The second phase will focus on the harmonization of scientific or mission-specific functions, such as grants management, scientific review of grant applications, or strategic planning, that will be kept at the IC level but may benefit from adoption of best practices. In some cases, this will allow a more equitable distribution of workload across NIH. In the last phase, NIH is planning to "cluster" activities at its Institutes and Centers (ICs), and the NIH Office of the Director (OD), into 7 Operational Service Centers over the next 24-36 months. These Centers will serve as cores to harmonize and integrate a variety of administrative support functions. In addition to these phases, Federal staff hiring at NIH is being coordinated centrally for consistency with recent levels, and will continue to be coordinated with the Optimize NIH plan.

Conclusion

The Nation's investment in NIH is borne from the recognition that a healthy population is a productive and thriving population. The benefits of NIH research may be felt in the near term through development of novel health interventions, but also continue well into the future, as transformations in the diagnosis, prevention, and treatment of disease today become standard practice tomorrow. For example, thanks in large part to NIH research, survival rates for respiratory distress syndrome in newborns have improved from 5 percent in the 1960s to 95 percent currently. The infants who now survive what was once a deadly condition will live to become productive adults, potentially with children of their own and on into future generations.

A healthier nation is a more productive and economically sound nation. The gains made in life expectancy in the U.S. for the period of 1970 to 2000 have been estimated to have an economic value of $95 trillion, about $3.2 trillion per year. Each permanent 1 percent reduction in cancer deaths alone has been approximated to have a value of nearly $500 billion to current and future generations of Americans. A full cure could be worth approximately $50 trillion—more than three times today's GDP.[27]

[27] http://www.ucema.edu.ar/u/je49/capital_humano/Murphy_Topel_JPE.pdf

Not only does NIH research benefit the economy through improvements in health, it is also a driver of industry, spurring innovation and growth in medical technology, pharmaceutical therapies, and biotechnology. The Human Genome Project alone likely resulted in as much as $1 trillion of economic growth, a 178-fold return on investment.[28]

Continued, targeted support of NIH is an investment in the well-being of the Nation now and into the future. Working with its many partners, NIH is well prepared to address current health needs and to capitalize on emerging scientific opportunities, the benefits of which will be felt by all generations to come.

[28] http://web.ornl.gov/sci/techresources/Human_Genome/publicat/2013BattelleReportImpact-of-Genomics-on-the-US-Economy.pdf

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 2019 budget request reflects the Agency's longstanding commitment to invest strategically using performance-based analysis, as emphasized in the Government Performance and Results Act (GPRA) (P.L. 103-62), as amended by 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.

Collectively, the NIH performance measures reflect the Agency's overall goals to: 1) advance the full continuum of biomedical research; 2) strengthen the scientific workforce and biomedical research infrastructure; 3) facilitate the communication of research findings and transfer of knowledge to other sectors for further development; and 4) enhance internal management processes, policies, and systems to support programmatic and organizational oversight. Furthermore, the measures support the Administration's goal of protecting and improving the health and well-being of the American people. In particular, NIH substantially contributes to HHS Strategic Goal 4 – Foster Sound, Sustained Advances in the Sciences. For example, in support of Objective 4.3 (Advance basic science knowledge and conduct applied prevention and treatment research to improve health and development) under Goal 4, NIH continues to support promising research with the goals of: 1) developing, optimizing, and

evaluating the effectiveness of nano-enabled immunotherapy (nano-immunotherapy) for one cancer type; 2) evaluating the safety and effectiveness of 1-3 long-acting strategies for the prevention of HIV; and 3) identifying risk and protective alleles that lead to one novel therapeutic approach, drug target, or pathway to prevention for late-onset Alzheimer's disease.

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.[29, 30] 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.

[29] 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.
[30] The seven standing working groups are: Extramural Activities, Diversity, Facilities, Management and Budget, Scientific Data Council, Administrative Data Council, and Data Science Policy Council.

ALL PURPOSE TABLE

(Dollars in Thousands)[2,3]	FY 2017 Final[1]	FY 2018 Annualized CR[1]	FY 2019 President's Budget[4]	FY 2019 President's Budget +/- 2018 Annualized CR
Total, NIH Program Level	**$34,229,139**	**$34,067,456**	**$34,766,707**	**$699,251**
Less mandatory and funds allocated from different sources:				
PHS Program Evaluation	824,443	818,844	741,000	-77,844
Mandatory Type 1 Diabetes Research	139,650	150,000	0	-150,000
Patient-Centered Outcomes Research Trust Fund (PCORTF)	0	0	124,349	124,349
Energy Employees Occupational Illness Compensation Program Act (EEOICPA)	0	0	55,358	55,358
Total, NIH Discretionary Budget Authority	**$33,265,046**	**$33,098,611**	**$33,846,000**	**$747,389**
Interior Budget Authority	77,349	76,824	53,967	-22,857
Total, NIH Labor/HHS Budget Authority	**$33,187,697**	**$33,021,788**	**$33,792,033**	**$770,245**
Number of Competing RPGs [5]	*10,123*	*8,656*	*9,084*	*428*
Total Number of RPGs [5]	*36,568*	*35,920*	*35,949*	*29*
FTEs [6]	*18,018*	*18,105*	*19,456*	*1,351*

[1] Excludes Ebola-related supplemental appropriations or transfers.

[2] Includes 21st Century Cures Act funding.

[3] Numbers may not add due to rounding.

[4] Includes funding and full-time equivalents (FTE) for proposed reorganizations supporting the establishment of the National Institute for Research on Safety and Quality (NIRSQ), National Institute for Occupational Safety and Health (NIOSH), and National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR).

[5] Annual levels exclude grants funded by NIOSH and NIDILRR.

[6] The FY 2019 total includes an estimated 18,105 FTE for existing NIH Institutes and Centers (IC). A projected 1,351 FTE are associated with new ICs established by the proposed reorganization (1,072 for NIOSH, 247 for NIRSQ---including 2 funded from the PCORTF mandatory account, and 32 for NIDILRR).

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	**FY 2018 Annualized CR**	**FY 2019 President's Budget[3]**	**FY 2019 +/- FY 2018**
Research Project Grants	$19,066.313	$18,894.528	-0.9%
Competing Average Cost (in thousands)	$518.305	$503.245	-2.9%
Number of Competing Awards (whole number)	8,656	9,084	4.9%
Estimated Competing RPG Success Rate	15.9%	16.0%	0.6%
Research Centers	$2,483.707	$2,482.718	0.0%
Other Research	$2,241.770	$2,192.596	-2.2%
Training	$839.805	$810.586	-3.5%
Research & Development Contracts	$2,896.751	$2,931.915	1.2%
Intramural Research	$3,787.681	$3,795.544	0.2%
Research Management and Support	$1,765.098	$1,757.337	-0.4%
Common Fund (non-add)	*$678.829*	*$598.781*	*-11.8%*
Buildings & Facilities Appropriation	$127.988	$200.000	56.3%
Other Mechanisms[1]	$858.343	$1,226.649	42.9%
Consolidations (except NIRSQ)	n/a	$474.834	n/a
Total, Program Level[2]	**$34,067.456**	**$34,766.707**	**2.1%**

[1] Includes Office of the Director-Other and Superfund Research activities funded from the Interior appropriation.

[2] Includes discretionary budget authority received from Labor/HHS appropriations (ICs) and the Interior appropriation (Superfund). Also includes mandatory budget authority derived from the Special type 1 Diabetes account (FY 2018 only) as well as Program Evaluation Financing.

[3] Includes funding for NIRSQ (except where noted), NIOSH, and NIDILRR associated with the proposed FY 2019 consolidation as well as PCORTF (NIRSQ) and EEOICPA (NIDILLR) mandatory accounts.