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 and supports biomedical research focused on fostering fundamental creative discoveries, innovative research strategies, and their applications towards improving human health.

As the Nation's premier biomedical research agency, NIH plays a critical role in advancing basic and clinical biomedical research to improve human health and pave the foundation for ensuring the Nation's economic well-being. NIH also works to develop, maintain, and renew scientific human and physical resources that will ensure the Nation's capability to prevent disease and disability. The biomedical research enterprise depends upon not only NIH's support of cutting-edge science and technology but also its wise investment of tax dollars. Through careful stewardship of public resources in pursuit of its mission, NIH strives to enhance the lives of all Americans.

Overview of Budget Request

Introduction

For FY 2020, the National Institutes of Health (NIH) requests a total program level of $34.4 billion, which is $4.9 billion less than the FY 2019 Enacted level. This budget reflects the need for fiscal austerity, but will still fuel NIH's mission to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life, and reduce illness and disability. As a leader of the biomedical research enterprise, NIH will leverage 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. Investing in new technology will push the boundaries of what is possible in imaging, device design, health monitoring, bioinformatics, and countless other areas. Today, 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 possibilities for groundbreaking approaches to better human health never have been greater.

The request of $34.4 billion incorporates investments to address the opioid epidemic, support development of a universal flu vaccine, implement the Strategic Plan for Data Science, and support cutting-edge intramural research by addressing the significant backlog of repair and improvements across NIH facilities. NIH's FY 2020 research investments will be guided by the NIH-Wide Strategic Plan for FY 2016-2020.[1]

The request proposes to move the highest priority activities of the Agency for Healthcare Research and Quality (AHRQ) into NIH as a new National Institute for Research on Safety and Quality (NIRSQ). The creation of NIRSQ, which was included in the Administration's June 2018 Government Reform Plan, would improve the coordination of research within the Department of Health and Human Services (HHS), with a continued emphasis on NIRSQ's integral role in support of the Secretary's priority to transfer the Nation's health care system to one that pays for value.

The request maintains funding for the Buildings & Facilities (B&F) account at $200 million, consistent with the FY 2019 Enacted level, and part of NIH's long-term effort to stem the deterioration of its facilities. NIH's Backlog of Maintenance & Repair is over $1.8 billion and is growing at an accelerating rate. An independent review of the facility needs of NIH's main campus will be completed this winter by the National Academies of Science, Engineering and Medicine.

From Inspiration to Innovation

NIH funds innovative research, supporting the best ideas submitted by talented researchers across the nation. Through these investments, NIH expands the frontiers of biomedical

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

knowledge, and brings hope of delivering new measures for prevention, treatments, and cures for our most challenging diseases and conditions. In FY 2020, NIH will focus on:

1. Developing Transformative Tools and Technology
   Advanced tools and techniques enable the development of faster and more accurate diagnostics, screening instruments, and treatment methods.

2. From Basic Science to Clinical Breakthroughs
   Fundamental science discoveries yield enormous long-term returns, providing the foundation for scientific advancement that leads to the clinical applications that ultimately help patients.

3. Exploring the Next Frontier in Biomedical Research
   Through ambitious research endeavors, harnessing the power of big data and revolutionary applications, and cultivation of the best and brightest biomedical research workforce, NIH will invest resources to ensure that the U.S. remains on the cutting edge of biomedical science.

Strategic investments in these areas will enable NIH and the U.S. to remain the world leader in biomedical research and to improve the health of all Americans.

Developing Transformative Tools and Technology
NIH-funded researchers are achieving transformative results through technology, and shedding new light on how biological systems function in health and disease. These insights are leading to faster, more accurate diagnostics, less invasive screening and treatment procedures, and hope for therapies and cures for previously intractable diseases. Gene editing, three-dimensional (3D) tissue printing, single cell biology, and neurotechnologies are just a few of the areas in which innovative discoveries are moving towards tangible results in delivering the promise of biomedical research for human health.

Research That Can Revolutionize the Practice of Medicine
Rapid, early, and accurate identification of disease improves the chances of treatment success and ultimately is key to saving lives. Recognizing that technology is key to delivering improved medical outcomes, NIH supports a diverse portfolio of research focused on developing cutting-edge diagnostic technologies. Examples include a miniature device that simultaneously detects and distinguishes between various tick-borne diseases, and another that captures mutated genetic material and proteins shed by brain tumors into the bloodstream for developing personalized treatments – both devices using just a single drop of blood. Technologies for non-invasively imaging the human body are also advancing rapidly, including a light-based, 15-second scan that could replace painful mammograms, and using screen-printing technology (like that used to print a logo on a T-shirt) to produce flexible MRI coils, custom-fit to patients, for faster imaging and better resolution. Other advances in the area of cancer research include the development of

fluorescent nanoparticles that can be used to identify and track breast cancer as it spreads through the body.

NIH-funded technological advances are pushing the boundaries of disease treatment and prevention. For example, an injectable hydrogel bandage is currently being developed that can stop potentially fatal internal bleeding and save lives in emergencies such as penetrating shrapnel wounds on the battlefield. Another team of engineers is developing a smart bandage designed to actively monitor the condition of chronic wounds and deliver appropriate drug treatments to improve the chances of healing. In addition, our ability to create complex artificial tissues, through technologies like 3D tissue printing, continues to progress, leading us closer to their use in transplants and other surgeries. NIH also invests in mobile health (mHealth) technology by arming smart devices with built-in sensors, making lifesaving healthcare more accessible. One application of mHealth that was designed by NIH researchers includes a reusable glucose meter system built into a smartphone case, providing people with diabetes with a mobile option for monitoring their glucose levels.

Other feats of biomedical engineering that have yielded advances include the use of painless microneedles for drug or vaccine delivery, which is now moving from concept to the clinic. NIH funded the development of a skin patch containing dissolving microneedles, and initial studies indicate that it will work as effectively as a regular shot in delivering the influenza vaccine. This influenza patch has the potential to eliminate the discomfort of an injection in addition to the benefits of being more convenient and less expensive than visiting a health care facility. Additional applications for microneedles are being piloted, including a pain-free skin patch that both measures and responds to sugar levels that could help manage type 2 diabetes.

Developing Gene Editing Technologies

Gene editing technologies equip researchers with tools for a broad range of research applications, including investigating gene function, developing better animal models to study specific human diseases, and diagnosing and fighting infectious diseases. Furthermore, through the ability to introduce, disrupt, or correct genes, these technologies show great promise for advancing therapies to treat genetic or acquired diseases including HIV, cancer, and genetic disorders such as sickle cell disease, muscular dystrophy, and hemophilia. One specific gene editing technique, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), is being studied to correct or compensate for the mutations that cause sickle cell disease, by editing the genome of stem cells derived from the bone marrow of an affected person. (It is important to point out that these gene editing therapeutic strategies will be applied to the appropriate cells of an affected child or adult – NOT to human embryos.) While these technologies hold tremendous potential, additional research is needed to improve the efficacy, specificity, and safety of gene editing systems. The ultimate goal is to develop approaches that could successfully treat any of the thousands of genetic disorders where the DNA misspelling is already known. In 2018, the NIH Common Fund launched a program called Somatic Cell Genome Editing[2] with these challenges

[2] https://commonfund.nih.gov/editing

in mind, and the research tools, assays, and delivery systems developed through this program will be made widely available to the research community. Ultimately, investment in this program will dramatically accelerate the development of these gene editing technologies and potentially reduce the time and cost required to develop new therapies for millions of patients with rare genetic disorders.

Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative
Launched in 2013, the NIH Brain Research through Advancing Innovative Neurotechnologies[3] (BRAIN) Initiative seeks to develop and apply technologies that will revolutionize our understanding of the human brain in health and disease. For example, BRAIN-funded investigators have developed a breakthrough method for identifying the gene expression patterns of different subtypes of brain cells that can identify what makes different types of cells unique. This approach identified new brain cell subtypes in the frontal cortex of the brain, thus expanding our understanding of the different neurons that contribute to brain cell diversity. The BRAIN Initiative also supports research on neurotechnologies with clinical applications, including deep brain stimulation (DBS). A team of BRAIN researchers successfully demonstrated the use of adaptive DBS in patients with Parkinson's disease using a fully implanted device that both senses brain activity and delivers electrical stimulation, allowing for fine-tuned stimulation in real-time with neuronal feedback, maintaining therapeutic efficacy and minimizing side effects. Finally, based on the successes of technologies emerging from the BRAIN Initiative, researchers are mapping functional circuits across the brain, paving the way for an unprecedented level of understanding of the human brain and improving human health. As the NIH BRAIN Initiative approaches the halfway point of its 10-year vision, NIH has launched an outreach and planning process for BRAIN 2.0, in order to ensure that the original strategic plan – *BRAIN 2025*[4] – keeps pace with the scientific and technological advances spurred by the Initiative.

From Basic Science to Clinical Breakthroughs
In pursuit of its mission, NIH invests more than half of its research budget in basic biomedical research, which provides the key for unlocking the secrets of how living systems function. With this substantial level of support, NIH lays the groundwork for discoveries that will ultimately lead to novel interventions, treatments, and cures. In fact, a recent study found that NIH funding contributed to published research associated with every single one of the 210 new drugs approved by the Food and Drug Administration (FDA) from 2010 through 2016. More than 90 percent of this NIH funding was for basic research.[5] Basic research results are driving improved diagnostic and treatment approaches for key diseases and conditions such as cancer, opioid addiction, and influenza, and NIH is working to ensure that clinical trials to test new approaches for a variety of diseases are available to everyone, including medically underserved and rural populations.

[3] https://www.braininitiative.nih.gov/
[4] https://www.braininitiative.nih.gov/2025/index.htm
[5] Galkina Cleary E. Contribution of NIH funding to new drug approvals 2010-2016. Proc Natl Acad Sci USA. 2018 115(10):2329-2334. PMID: 29440428.

Changing the Course of Childhood Cancer

Enormous strides have been made in the treatment of childhood acute leukemia, where the cure rate now stands at well over 90 percent. But the science of understanding other types of pediatric cancer is especially challenging, and too many children and adolescents still die from rare brain tumors, sarcomas, and other malignancies. Many others endure lifelong adverse effects from their cancers or their treatment.

In FY 2020, NIH will invest an additional $50 million above the FY 2019 level to accelerate research on pediatric cancer. This investment reflects the first year of a new 10-year, $500 million initiative launched by the President in the 2019 State of the Union address. The initiative will expand upon current progress to enhance drug discovery and clinical trials and improve our understanding of the biology of all pediatric cancers through a new, national data resource. The data resource will support research to develop new, more effective, and safer treatments for childhood cancers, and will complement ongoing research within the National Cancer Institute (NCI) and the Cancer Moonshot. Through this initiative, NCI will aggregate data from pediatric cancer cases and coordinate with others that maintain data sets to create a comprehensive, shared resource to support childhood cancer in all its forms. This knowledge, spanning from basic biology to clinical outcomes, can provide a path for changing the course of cancer in all children.

Understanding and Harnessing the Immune System

Basic research continues to deliver valuable insights into the relationship between the immune system and a plethora of complex conditions, which in turn help inform the development of new treatments. For example, recent research indicates that the microbiome, comprising bacteria and other microbes that live in or on the body, likely interacts with the immune system to influence health and susceptibility to diseases like obesity, diabetes, and autoimmune disorders. Researchers also are investigating how the microbiome may interact with the immune system to influence the development of cancer or Alzheimer's disease. Findings from these and similar studies could lead to new therapies that interrupt or reverse disease progression.

The rapidly advancing field of cancer immunotherapy builds on NIH's long-term investment in basic research on the immune system. Immunotherapies reflect a new tool in our fight against cancer, as they focus on harnessing the body's own immune system to fight off the disease. Investment in cancer immunotherapy, including resources from the Beau Biden Cancer Moonshot,[6] will help accelerate these efforts. Current research involving one type of immunotherapy, called adoptive cell transfer (ACT)—in which tumor-killing immune cells are harvested and grown to large numbers in the laboratory, then infused back into the patient—shows the potential to target diverse tumors based on their DNA mutations rather than the specific type of cancer. The use of ACT in an ongoing Phase 2 clinical trial has yielded positive results for potential treatment of a variety of previously incurable metastatic solid tumors, including breast, liver, and colorectal cancer. Other immunotherapy treatments are in earlier preclinical stages of development. For example, one exciting approach involves tumor vaccination, in which treatments are injected directly into a tumor and then not only lead to

[6] https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative

destruction of that tumor, but also other tumors of the same type throughout the body. Because a tumor vaccine does not depend on knowing the unique characteristics of a tumor, the technique may potentially be applied to many forms of cancer.

NIH is also working to identify which patients are most likely to respond to immunotherapy treatments. Researchers recently found a biomarker that may identify patients who will benefit from a type of ACT immunotherapy called CAR T-cell therapy. If confirmed in larger studies, the biomarker could be used to guide treatment options. Recognizing the importance of identifying and validating biomarkers to advance new immunotherapy treatments, NIH launched the Partnership for Accelerating Cancer Therapies (PACT) in October 2017 as part of the Cancer Moonshot. PACT is a five-year public-private research collaboration between NIH and 12 biopharmaceutical companies, with the aim of developing biomarkers that can predict responses and advance cancer immunotherapy.

Helping to End Addiction Long-term (HEAL) Initiative
More than 2 million Americans have an opioid use disorder (OUD), and millions more misuse opioids by taking opioid medications longer or in higher doses than prescribed. To help bring scientific solutions to this crisis, and to provide safe and effective options for the more than 25 million Americans who suffer from daily chronic pain, NIH launched the Helping to End Addiction Long-term (HEAL) Initiative.[7] Introduced in April 2018, and funded in the FY 2018 Congressional appropriation, this initiative will direct an additional $500 million annually towards research across NIH aimed at improving treatments for opioid misuse and addiction, and enhancing pain management strategies. Through HEAL, NIH is building on basic science discoveries to accelerate the development of novel medications and devices to treat all aspects of the opioid addiction cycle, including chronic use, withdrawal symptoms, craving, relapse, and overdose. In addition, studies on integrating prevention and treatment approaches into practice, including the HEALing Communities study,[8] will inform understanding of how the implementation of promising and evidence-based strategies and treatments can decrease OUD and overdose deaths. The FY 2020 request supports a total of $1.3 billion for opioids and pain research across NIH, including $500 million for the HEAL Initiative.

Long-lasting solutions to the opioid crisis will require additional pharmacological and non-pharmacological options for pain management -- to protect patients from the risk of opioids. NIH is working with experts from the biopharmaceutical industry and federal partners to develop a data sharing collaborative, new biomarkers for pain, and a clinical trials network for testing new pain therapies, as well as to enhance clinical practice for pain management. Launched in FY 2019, the Acute to Chronic Pain Signatures program from the NIH Common Fund will collect neuroimaging, -omics (high-throughput biomedical experiments), sensory testing, and psychosocial data from patients with acute pain associated with a surgical procedure or acute musculoskeletal trauma. Through this study, NIH will seek to predict which patients will

[7] https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative
[8] https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative/heal-initiative-research-plan

develop long-lasting chronic pain, and guide precision acute pain management approaches to seek to block that transition.

To improve both short- and long-term developmental outcomes for infants with Neonatal Abstinence Syndrome (NAS)/Neonatal Opioid Withdrawal syndrome (NOWs), HEAL will determine the best approaches to identify and treat newborns exposed to opioids by expanding the Advancing Clinical Trials in Neonatal Opioid Withdrawal syndrome (ACT NOW) pilot studies. ACT NOW will assess NOWs prevalence and the variation in current approaches to clinical management, as well as develop common protocols for conducting large-scale studies across the country, particularly in areas hardest hit by the opioid epidemic. Results from the study will be used to conduct clinical trials to determine best clinical practices, including assessment of drug-free treatment approaches and currently used medications.

In the current fiscal year, NIH will rapidly expand on these efforts with a variety of new projects in the HEAL Initiative, such as research on prevention approaches for adolescents and young adults at risk for addiction, and long-term evaluation of infants born dependent on opioids. Other projects will focus on treatment of OUD, including optimal duration of medications and the study of behavioral interventions in addition to medication. Non-pharmacological strategies for pain management and novel non-addictive pain medications also will be explored through clinical studies of different pain conditions and the collection of real-world data. HEAL Initiative research projects will be conducted in partnership with colleagues across government, the private sector, and in communities nationwide, ensuring that all hands are on deck to respond to the crisis of pain and addiction.

Working Towards a Universal Influenza Vaccine

NIH-supported research is helping advance understanding of how flu (influenza) strains emerge, evolve, infect, and cause disease. These research results are informing design of new and improved therapies, diagnostics, and vaccines, including a "universal" influenza vaccine. Circulating and emerging influenza viruses pose an ever-present public health threat and place substantial health and economic burdens on the U.S. and the world. Annual influenza vaccination remains the most effective way to reduce influenza morbidity and mortality. However, traditional vaccine development strategy relies heavily on predicting which strains will be in circulation each year, which is a suboptimal approach when dealing with constantly evolving and newly emerging virus strains. NIH is investing in ways to make seasonal flu vaccines longer lasting and more effective in order to better protect the population. At the same time, to move toward durable protection against multiple influenza strains—including those that may pose a pandemic threat—NIH is making parallel efforts in rational design of a universal influenza vaccine.

In FY 2018, NIH unveiled a strategic plan to guide future basic, translational, and clinical research investments in areas essential to creating a safe and effective universal influenza vaccine.[9] Along this path, NIH is funding basic research to understand the transmission, natural history, and disease process of influenza, in addition to characterizing how immunity occurs and how to tailor vaccination responses to both achieve immunity and extend the duration of protection. By applying cutting-edge vaccine technology, NIH is modernizing vaccine development approaches in pursuit of its goal to design a broadly protective flu vaccine for all ages. Several universal flu vaccine strategies are already being tested in NIH-supported clinical trials.

Spurring New Models for Drug Discovery

Significant resources are invested in developing new drugs, yet 90 percent of candidate drugs are later found to be either unsafe or ineffective in humans. Discovering which drugs are ineffective or toxic earlier in the drug development process would save time and money. Propelled by basic and preclinical translational research, and in collaboration with the Defense Advanced Research Projects Agency (DARPA) and the FDA, the Tissue Chip for Drug Screening Program[10] is among the NIH-supported initiatives focused on developing new tools and resources to facilitate this process. Tissue chips are engineered 3D platforms that are lined with living human cells and designed to replicate the complex biological functions of a specific human organ, such as the lung, liver, kidney, or heart. The ultimate goal of the program is to accelerate the translation of basic discoveries into the clinic by allowing researchers to test candidate drugs across model organs before doing any testing in humans. In FY 2017, NIH funded 13 two-year awards totaling about $15 million per year to develop 3D microphysiological system platforms that model human disease. For example, NIH-funded scientists used stem cells to create an adult-like cardiac model that mimics human heart functionality. This model can be used to improve predictions of the effects that drugs or environmental factors have on the actual heart tissue of a patient. NIH-supported scientists also have used stem cells and tissue chips to mimic conditions in early spinal cord development that enabled the discovery that blood vessels in the brain can trigger the growth and maturation of spinal cord neurons during development. These insights are important in understanding neurodegenerative diseases like amyotrophic lateral sclerosis (ALS) and hold the hope of finding custom, effective treatments for patients. Future phases of this group of awards will include plans to use the models for efficacy and safety testing of compounds to treat or prevent diseases.

IDeA States Pediatric Clinical Trials Network

Children living in rural and medically underserved states are less likely to be enrolled in clinical trials than children living in other states across the nation. To address this gap, in FY 2016 NIH created the Institutional Development Award (IDeA) States Pediatric Clinical Trials Network (ISPCTN), a component of the National Pediatric Research Network, under the Environmental Influences on Child Health Outcomes (ECHO) Program. The goal of the IDeA program is to broaden geographic distribution of NIH funding, and the goals of the ISPCTN include providing medically underserved and rural populations with access to cutting-edge clinical trials and

[9] Erbelding EJ et al. A Universal Influenza Vaccine: The Strategic Plan for the National Institute of Allergy and Infectious Diseases. J Infect Dis. 2018 Jul 2;218(3):347-354. PMID: 29506129

[10] https://ncats.nih.gov/tissuechip

applying findings from other relevant pediatric cohort studies to children in IDeA state locations.[11] The ISPCTN will also build national pediatric research capacity by providing professional development opportunities for faculty and their support teams as well as supporting investment in infrastructure. In FY 2020, NIH will increase ECHO funding by $15 million to continue the ISPCTN and support studies such as the multi-site clinical trial on the Pharmacokinetics of Understudied Drugs Administered to Children per Standard of Care (POPS) Study, which evaluates the dosing, safety, and efficacy of drugs that are commonly prescribed to children. The ISPCTN is also partnering on ACT NOW pilot studies to develop best practices for treatment of Neonatal Opioid Withdrawal syndrome, as well as advancing clinical trial protocols for a study that aims to decrease pediatric obesity rates in rural areas through use of mobile health technology.

Exploring the Next Frontier in Biomedical Research

Biomedical research aims to push the frontier of knowledge, and success relies on constantly pursuing the next scientific question. NIH will continue to invest in people, programs, and technology with this goal in mind, consistently striving for breakthroughs that culminate in improvements in human health and wellbeing. From harnessing new technologies such as big data analytics and artificial intelligence to supporting the next generation of researchers, NIH will invest its resources to ensure that the U.S. remains on the cutting edge of biomedical research.

Making Sense of Big Data

NIH has initiated a variety of programs to advance scientific discovery and cures by leveraging the incredible growth in the volume, speed of delivery, and complexity of large biomedical datasets. In June 2018, NIH released the Strategic Plan for Data Science[12] (Plan). The Plan articulates NIH's vision for making big data sustainable, interoperable, accessible and usable for the broader community by 1) optimizing data infrastructure, 2) modernizing data resources, 3) advancing data management, analytics, and tools, 4) promoting workforce development, and 5) enhancing policy stewardship and sustainability. NIH is now mapping out implementation activities, which will intensify over the next year. NIH is also creating a new position–the NIH Chief Data Strategist–to collaborate closely with key stakeholders and lead implementation of the Plan.

Additionally, NIH is focused on the promise of artificial intelligence (AI) and machine learning (ML) for catalyzing advances in basic (e.g., image interpretation, neuroscience, genomic variants and disease risk, gene structure, and epigenomics) and clinical research (e.g., robotic surgery, natural language processing of electronic health record data, inferring treatment options for cancer, reading radiology results). NIH recognizes that there are many areas of biomedical research where novel computing, machine intelligence, and deep learning techniques have the potential to advance human health. NIH is committed to pushing those frontiers. For example, in July 2018, NIH hosted a high-level workshop, "Harnessing Artificial Intelligence and

[11] https://www.nigms.nih.gov/research/crcb/IDeA/Pages/default.aspx
[12] https://datascience.nih.gov/sites/default/files/NIH_Strategic_Plan_for_Data_Science_Final_508.pdf

Machine Learning to Advance Biomedical Research" which brought together experts from across the community to examine new directions and challenges in AI and ML and identify ways NIH can contribute to solving these obstacles. NIH has convened a new working group of the Advisory Committee to the Director to further these goals.

All of Us: Creating a National Research Resource to Advance Precision Medicine

Precision medicine represents a key frontier of human health and disease, taking into account individual differences in lifestyle, environment, and biology to enable prevention and treatment strategies tailored to individuals. Initiated in FY 2016, the NIH *All of Us* Research Program,[13] a key element of the Precision Medicine Initiative (PMI), is a historic effort to gather data from one million or more people living in the U.S. to accelerate research and improve health. Unlike research studies that are focused on a specific disease or population, *All of Us* will serve as a national research resource to support thousands of studies, covering a wide variety of health conditions. *All of Us* also represents a new frontier in the way in which research is conducted, through engaged participants and open, responsible data sharing. *All of Us* is working to capitalize on recent advances in genomics, big data analytics, environmental science, and other technologies to revolutionize biomedical research and increase precision medicine prevention and treatment options for individuals and their communities.

National enrollment for *All of Us* launched in May 2018, after extensive design and testing of the many systems involved. By late January 2019, more than 175,000 people have registered with the program as the first step in the participant journey. More than 100,000 participants have completed all the steps in the initial protocol (i.e., consented, agreed to share data from their electronic health records, completed the first three surveys, and provided physical measurements and biospecimens). Greater than 75 percent of these participants are from communities that have been historically underrepresented in biomedical research, and nearly 50 percent are from racial and ethnic minority groups. To encourage enrollment of diverse populations, NIH has created a network of community engagement partners to help with outreach and building trust in these communities. NIH also issued three Genome Center awards in September 2018 to generate genotype and whole genome sequence data from participants' biospecimens—a critical component in the program's research platform. Additionally, *All of Us* is planning a pilot on the responsible return of genetic information to participants, which will include education and genetic counseling, as part of the program's commitment to make participant data available to participants themselves.

Supporting the Next Generation of Researchers

NIH leadership, scientists in the research community, Congress, and the public have grown increasingly concerned about the long-term stability of the biomedical research enterprise. Over time, the number of applications seeking NIH support has increased faster than available funding, which may contribute to early-stage career scientists turning away from careers in research. But they are our future, and we cannot afford to lose them.

[13] https://allofus.nih.gov/

In August 2017, NIH launched the Next Generation Researchers Initiative (NGRI). This initiative – which also responds to provisions in the 21st Century Cures Act – addresses challenges faced by early-stage investigators trying to embark upon and sustain independent research careers.[14] As a key part of the initiative, NIH is prioritizing meritorious applications from early stage investigators seeking their first award, and also for investigators currently supported by NIH who are at risk of losing all research support. Moreover, in their award decisions, NIH Institutes and Centers will consider factors such as emerging areas of scientific inquiry, the distribution of the scientific portfolio, and the projected needs of the scientific workforce, including enhanced workforce diversity.

Using a systems-oriented, data-driven approach, an NGRI working group, operating under the Advisory Committee to the NIH Director, made recommendations for change, and will continue to monitor the success of the new initiative. Further, NIH is currently assessing recommendations in a related report from the National Academy of Sciences,[15] released in April 2018, which suggested that funders and institutions should consider addressing barriers that may extend periods of training, time to independence, or impede sustained success in research. NIH will incorporate guidance from both groups in the future design, testing, implementation, and evaluation of policies to ensure the success of the next generation of talented biomedical researchers. The FY 2020 Budget includes a dedicated $100 million in the Office of the Director for NGRI to supplement efforts undertaken by the Institutes and Centers with their own appropriations.

The request will reduce the direct cost of research by capping the percentage of an investigator's salary that can be paid with NIH grant funds at 90 percent. This administrative policy will complement the statutory provision that limits salaries paid through a grant or other extramural mechanism to a rate not in excess of Executive Level II, which the Budget reduces to Executive Level V, and will help target available funding to support the highest priority research on diseases that affect human health.

Conclusion

NIH is at the vanguard of biomedical research, leading the world in support of groundbreaking science in the 21st Century. By strategically investing in scientific opportunities such as those described above, NIH will help ensure the U.S. remains at the forefront of innovation and discovery. In striving to achieve its mission, NIH also operates as a powerful economic engine that drives industry and stimulates investment and growth in pharmaceutical, biotechnology, and medical device companies. The fruits of NIH research–a healthier, longer-living population–also have substantial economic benefits.[16] Continued, targeted support of NIH is therefore an

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[14] https://grants.nih.gov/grants/guide/notice-files/not-od-17-101.html
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-214.html

[15] https://www.nap.edu/catalog/25008/the-next-generation-of-biomedical-and-behavioral-sciences-researchers-breaking

[16] https://ucema.edu.ar/u/je49/capital_humano/Murphy_Topel_JPE.pdf

investment not only in the health and well-being of all Americans, but also in the economic health of our country.

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 2020 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 Institutes and Centers (ICs) and the Office of the Director (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. ICs and OD offices carry out priority setting, performance monitoring, and progress reviews, and also make 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.

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, in which scientific excellence is assessed, consists of chartered scientific review groups composed of outside experts in particular scientific disciplines. The second level, in which public health relevance is assessed, is conducted by 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 with the greatest potential of furthering NIH's mission.

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.[17, 18] 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.

[17] 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.
[18] 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)[1,2,3,4]	FY 2018 Final	FY 2019 Enacted	FY 2020 President's Budget	FY 2020 +/- FY 2019
Total, NIH Program Level	**$37,224,080**	**$39,306,349**	**$34,367,629**	**-$4,938,720**
Less mandatory and funds allocated from different sources:				
PHS Program Evaluation	922,871	1,146,821	741,000	-405,821
Type 1 Diabetes Research	150,000	150,000	150,000	0
Total, NIH Discretionary Budget Authority	**$36,151,209**	**$38,009,528**	**$33,476,629**	**-$4,532,899**
Interior Budget Authority[5]	77,349	77,349	66,581	-10,768
Total, NIH Labor/HHS Budget Authority	**$36,073,860**	**$37,932,179**	**$33,410,048**	**-$4,522,131**
Number of Competing RPGs[6]	*11,461*	*11,675*	*7,894*	*-3,781*
Total Number of RPGs[6]	*39,354*	*41,389*	*38,565*	*-2,824*
FTE[7]	*17,532*	*18,101*	*18,339*	*238*
NEF[8]	*NA*	*96,000*	*NA*	*NA*

1 Excludes Ebola-related and hurricane-related supplemental financing.

2 Includes 21st Century Cures Act funding.

3 Numbers may not add due to rounding.

4 Figures for FY 2020 reflect the proposed consolidation of Agency for Healthcare Research and Quality (AHRQ) activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ). Figures for FY 2018 and FY 2019 do not include AHRQ.

5 This activity was operating under an FY 2019 Continuing Resolution at the time the budget estimates were prepared.

6 Figures for FY 2020 include NIRSQ. Figures for FY 2018 and FY 2019 do not include AHRQ.

7 FTE levels exclude 4 NIH FTEs funded by PHS trust funds in FY 2018 through FY 2020 and 7 FTEs funded by the Patient-Centered Outcomes Research Trust Fund in FY 2020. Figures for FY 2018 and FY 2019 do not include AHRQ.

8 Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on December 4, 2018; HHS has not yet notified for FY 2020.

Impact of Budget Level on Performance

Programs and Measures (Dollars in Millions, except where noted)	**FY 2019 Enacted**	**FY 2020 President's Budget**[3]	**FY 2020 +/- FY 2019**
Research Project Grants	$22,579.392	$19,544.723	-13.4%
Competing Average Cost (in thousands)	$540.593	$471.985	-12.7%
Number of Competing Awards (whole number)	11,675	7,894	-32.4%
Estimated Competing RPG Success Rate	20.3%	13.5%	-33.5%
Research Centers	$2,688.141	$2,217.953	-17.5%
Other Research	$2,489.688	$2,209.720	-11.2%
Training	$888.955	$801.873	-9.8%
Research & Development Contracts	$3,132.619	$2,795.430	-10.8%
Intramural Research	$4,129.550	$3,633.805	-12.0%
Research Management and Support	$1,898.356	$1,739.376	-8.4%
Common Fund (non-add)	*$619.166*	*$532.967*	*-13.9%*
Buildings & Facilities Appropriation	$200.000	$200.000	0.0%
Other Mechanisms[1]	$1,299.648	$1,224.749	-5.8%
Total, Program Level[2]	**$39,306.349**	**$34,367.629**	**-12.6%**

[1] Includes Office of the Director-Other, Buildings and Facilities funding in the National Cancer Institute, 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 Type 1 Diabetes account and Program Evaluation Financing.

[3] Mechanism distribution includes funding for NIRSQ in FY 2020.