On behalf of the National Institutes of Health (NIH), I am transmitting the Congressional Justification of the NIH request for the fiscal year (FY) 2021 budget. This request for a $38.7 billion total program level is critical in supporting 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. Importantly, this budget request enables the NIH to catalyze economic growth throughout the Nation by allowing researchers in every state to transform inspiration into innovation.

The NIH FY 2021 budget ensures that NIH can prioritize innovation to develop transformational tools and technologies, discover new clinical breakthroughs, and advance the next frontier of biomedical research. NIH-funded researchers maintain global leadership in ingenuity, creating much-needed diagnostics and treatments for currently intractable diseases and conditions. With the advancement of emerging technologies such as gene-editing, 3D tissue printing, artificial intelligence, single-cell biology, and neurotechnologies – to name a few – innovative discoveries are the key to transforming the promise of biomedical research into tangible hope for patients.

To advance the NIH mission, the FY 2021 budget will continue its long-standing commitment to investing in basic research and the arc of translation into clinical practice. Fundamental research is the key to unlocking the secrets of how living systems function and remains the foundation for the development of novel treatments and cures. For instance, NIH-supported basic research continues to push the frontier in understanding and treating HIV, which is leading to the development of new effective treatments, rapid diagnostics, and other approaches that now allow HIV-infected individuals to live a nearly normal lifespan. Basic research also serves as the foundation for the NIH Helping to End Addiction Long-term (HEAL) Initiative, which aims to curb the opioid epidemic and provide non-addictive alternatives for individuals who suffer from chronic pain.

Importantly, the FY 2021 budget allows NIH to secure the Nation's investment in the current workforce and the next generation of biomedical research scientists. More than 80 percent of the NIH's funding is awarded for extramural research, largely through almost 50,000 competitive grants to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every state. Additionally, the Next Generation Researchers Initiative provides NIH with an opportunity to address the challenges of tomorrow's scientific workforce. As such, NIH plans to prioritize meritorious applications from early-stage investigators and develop evidence-based strategies to support mission-specific workforce issues.

In conclusion, the FY 2021 budget provides resources for NIH, and the researchers around the country it supports, to continue to develop, maintain, and renew scientific activities that will

enhance our ability to prevent and ultimately cure disease. I look forward to discussing the FY 2021 budget request.

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

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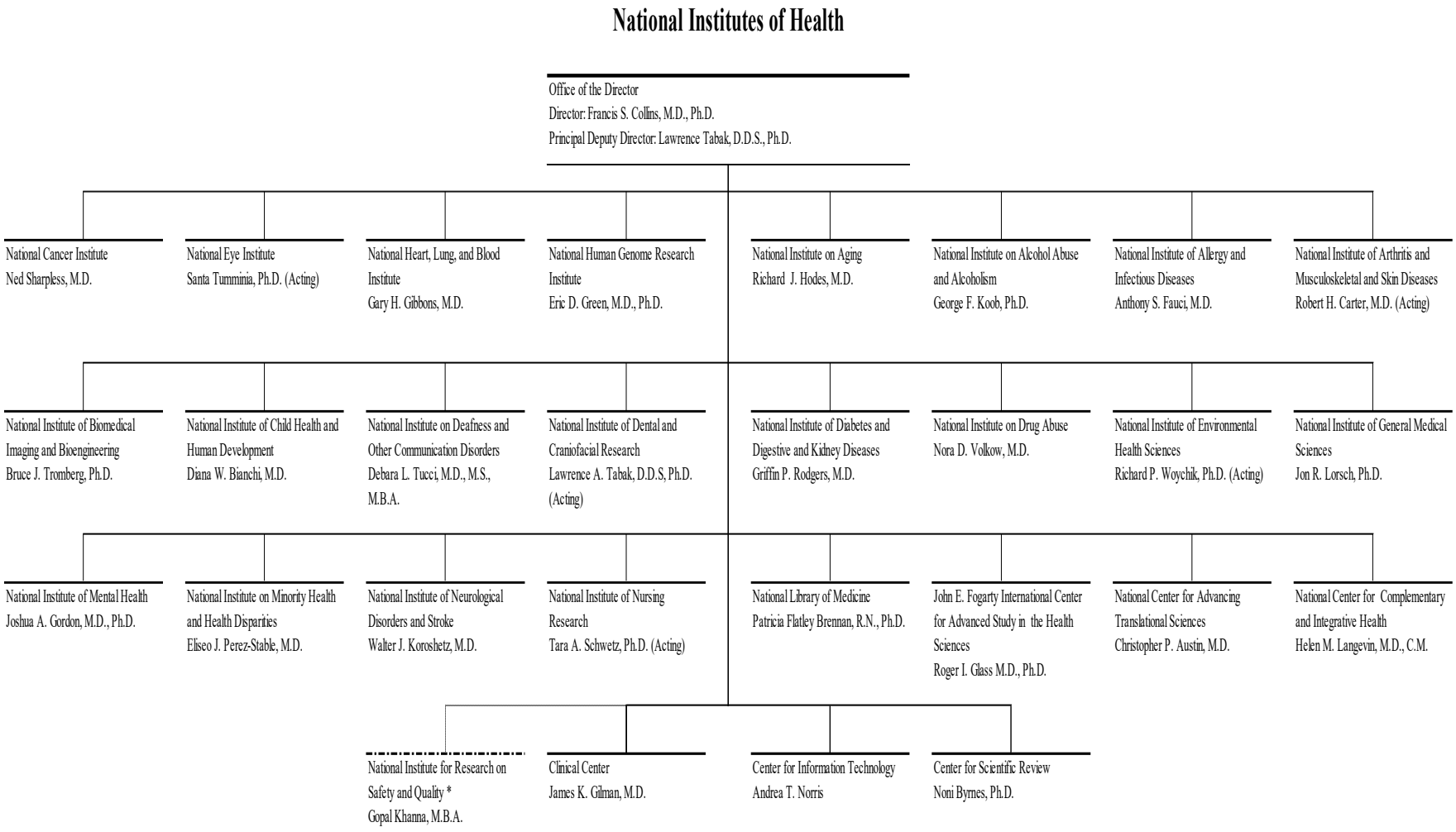

* The FY 2021 Budget proposes to consolidate the highest priority activities of the Agency for Healthcare Research and Quality within NIH as the National Institute for Research on Safety and Quality

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 drive 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 2021, the National Institutes of Health (NIH) requests a total program level of $38.7 billion, which is $3.0 billion less than the FY 2020 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 $38.7 billion incorporates investments to address several national priorities, including combatting the opioid epidemic, eradicating HIV, supporting neonatal research, developing novel approaches to treating sickle cell disease, supporting the Childhood Cancer Data Initiative, increasing investments to develop a universal influenza vaccine, improving prevention and treatment of tick-borne diseases, continuing the precision medicine initiative, developing new approaches to address chronic disease with artificial intelligence, and establishing a consortium charged with innovating large-scale gene vector production.

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 Buildings & Facilities (B&F) account budget request is $300.0 million, a $100.0 million increase over the FY 2020 Enacted level, and part of NIH's long-term effort to stem the deterioration of its facilities. NIH's Backlog of Maintenance & Repair (BMAR) is approximately $2.1 billion. An independent review of the facility needs of NIH's main campus by the National Academies of Sciences, Engineering, and Medicine that was released last August highlights pressing campus-wide infrastructure needs and recommends improvements to NIH's capital planning and funding processes, including prioritizing projects of highest functional research value. In addition to the $100.0 million increase, the Budget proposes a general provision that would permit NIH to supplement the B&F account through a new transfer authority. Institute and Center appropriations generally have a one-year period of availability, which is not sufficient for construction projects, and the new transfer authority would provide the funds with the same five-year period of availability as funds appropriated directly to the B&F

account. Together, these changes would allow NIH to halt the growth of BMAR and provide the necessary infrastructure for cutting-edge science.

In striving to achieve its mission, NIH supports a world-class research workforce that aims to increase understanding of the fundamental nature of disease. The knowledge from this research can then be harnessed to move the biomedical research enterprise forward, ultimately benefiting the human and economic health of our country.

Supporting and Training World-Class Researchers

More than 80 percent of the NIH's funding is awarded for extramural research, largely through almost 50,000 competitive grants to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every state. A recent study showed that NIH directly supported the training of more than 9,500 pre-doctoral and almost 5,900 post-doctoral fellows through training grants.[1] To date, 156 NIH-supported researchers, including 24 intramural investigators, have been awarded the Nobel Prize.[2] The Lasker Prize, which is often called "America's Nobel," recognizes researchers and clinicians for their contributions to medicine and has been awarded to 195 NIH-supported researchers, including 33 intramural investigators.[3]

Harnessing New Knowledge for Biomedical Advances

There are many examples of how NIH-supported research has helped build a solid foundation for new innovations or discoveries. For example, researchers have identified more than 25 additional genes involved in Alzheimer's disease and what role they may play. Discovering these pathways could help identify potential targets for drug and non-drug interventions to stop or prevent the disease.[4] NIH-supported research has also led to a significant reduction in organ transplantation rejection, identified specific disease-related genes that could be targeted by cutting-edge gene therapies, and led to the development of methods to transform induced pluripotent stem cells into neurons that may be useful in repairing brain injuries. In addition, a suite of vaccines commonly used to protect newborns, including the *Haemophilus influenzae* B vaccine, was developed from discoveries made possible by NIH support.

Management Efficiencies

NIH has implemented and continues to pursue efficiencies in its internal operations, in order to use taxpayer dollars wisely and maximize the intramural and extramural research that can be funded within available appropriations. One area of focus is category management, which leverages the Government's combined purchasing power to obtain the best value in its acquisitions. Another focus area for cost savings is energy efficiency. Investments in the NIH Central Utility Plant and building-specific energy efficiencies reduced facility energy consumption through FY 2018 by 29 percent from the 2003 baseline, the equivalent of

[1] www.ncbi.nlm.nih.gov/pubmed/26625903
[2] www.nih.gov/about-nih/what-we-do/nih-almanac/nobel-laureates
[3] www.nih.gov/about-nih/what-we-do/nih-almanac/lasker-awards
[4] www.nia.nih.gov/about/advances-alzheimers-disease-related-dementias-research

$54 million in savings annually. Two large Utility Energy Savings Contracts (UESCs) covering the Bethesda campus were executed in FY 2019, leading to further savings. NIH will continue to identify and pursue activities to improve management of the biomedical research enterprise.

With an Eye Towards the Future: The Arc of Biomedical Research

Advances in preventative measures, diagnostics, and treatment don't happen overnight. Typically, they are built upon knowledge amassed over time. Below are a few compelling examples of how NIH supports the fundamental understanding of human disease in order to positively influence human health.

Understanding and Treating Drug Misuse and Addiction

Over the last four decades, NIH-supported research has revolutionized our understanding of drug use and addiction, driving a new understanding of the neurobiological, genetic, epigenetic, social, and environmental factors that contribute to substance use disorders. These advances have helped to transform how drug use and addiction are conceptualized. Society's responses to drug use have often been shaped by the misconception that people with addictions are morally flawed and lacking in willpower, resulting in an emphasis on punishment rather than prevention and treatment. Today, thanks to groundbreaking scientific discoveries about the brain and its role in addiction, society's views are changing in ways that will enable us to respond more effectively to the problem. Recent scientific advances helped us gain an understanding of addiction as a chronic, relapsing disease. Scientists, through sophisticated neuroimaging techniques, have identified the specific sites of action in the brain where many of the major drugs of abuse have initial effect.

Many of the current tools at our disposal are being used to combat the public health crisis posed by opioid misuse and addiction in America. More than 47,000 Americans died of opioid overdose in 2017, and over 2 million Americans live with an addiction to opioids. Moreover, more than 50 million Americans suffer from chronic pain, and of those, 25 million live with daily chronic pain and lack effective and safe non-opioid options for pain management. These staggering numbers are likely underestimated. With the full support of the Administration, NIH launched an integrated set of research initiatives, collectively called the Helping to End Addiction Long-term (HEAL) initiative, to provide scientific solutions to the opioid crisis and offer new hope for individuals, families, and communities affected by this devastating crisis.

Congress initially provided $500 million in funding for HEAL in FY 2018, split equally between the National Institute on Drug Abuse (NIDA) and National Institute of Neurological Disorders and Stroke (NINDS), along with authority to transfer funding to other Institutes and Centers (ICs) in support of the initiative. The same level of funding was provided in the FY 2019 and FY 2020 enacted appropriations. NIH allocated $515.7 million to HEAL in FY 2019 and $532.6 million in FY 2020. The FY 2020 funding augments the estimated $900 million in resources in FY 2020 for base (non-HEAL) research related to opioids and pain across NIH. The FY 2021 request maintains a total of $1.4 billion for opioids and pain research across NIH, including $532.6 million for HEAL. In addition, NIH will allocate $50 million to support

research to develop medication-assisted treatment and evidence-based psychosocial treatment as part of the Department's priorities and strategies for reducing the use of methamphetamines.

Recently, NIH awarded 15 grants to form the Justice Community Opioid Innovation Network (JCOIN) to support research on quality addiction treatment for opioid use disorder in criminal justice settings nationwide. The awards, totaling approximately $141.3 million, will support the multi-year innovation network, including research institutions and two centers that will provide supportive infrastructure. JCOIN will establish a national network of investigators collaborating with justice and behavioral health stakeholders to research promising interventions and other approaches to improve the capacity of the justice system to respond to the opioid crisis. Awarded research centers will study evidence-based medications, behavioral interventions, digital therapeutics, and comprehensive patient-centered treatments in 15 states and Puerto Rico.

The scientific knowledge that we have, and will continue to accumulate, will transform the way we treat addiction and prevent drug misuse. Some of these advancements could include vaccines to sustain drug abstinence, refined prevention and treatment interventions targeted to individual risk, and a new generation of emerging medications.

Eliminating HIV/AIDS

The Presidential initiative *Ending the HIV Epidemic: A Plan for America* aims to reduce new HIV infections in the United States by 75 percent by 2025 and by 90 percent by 2030. As part of this initiative, FY 2020 enacted appropriations included $6 million for NIH to expand the Centers for AIDS Research (CFAR) within the National Institute for Allergy and Infectious Diseases (NIAID) to perform several pilot studies to jump-start evidence-based research on new strategies for the delivery of integrated prevention and treatment. The FY 2021 budget includes an additional $10 million in funding, for a total of $16 million, to support this initiative by leveraging the CFAR's pilot data to design and evaluate effective, sustainable systems for the implementation of prevention and treatment interventions, with a focus on implementing strategies at scale that will be the most effective. This will ensure that promising strategies, such as the use of long-acting sustained-release medications for prevention and treatment, are brought rapidly into clinical use.

NIH-supported basic research has allowed us to gain a deep understanding of the biology of HIV. This, in turn, has led to the development of effective treatments, rapid diagnostics, and other approaches that now allow HIV-infected individuals to live a nearly normal lifespan. This is an amazing accomplishment considering that at the beginning of the HIV epidemic, there were limited treatment options, aside from palliative care, and infection meant death.

An especially tragic result of the HIV epidemic was the transmission of HIV from infected mothers to their infants. A landmark NIH-funded study demonstrated that the antiretroviral drug AZT reduced by two-thirds the risk of HIV transmission from an HIV-infected mother to her infant. Current antiretroviral drug therapy has now nearly eliminated that risk in the United States.

Research has also firmly established that people who take antiretroviral therapy daily as prescribed, and who achieve and maintain undetectable levels of HIV in their blood, cannot sexually transmit the virus to others. In short, "undetectable equals untransmittable."[5] While these advances are undeniably positive, they do require staying on medication for life. That makes finding a cure for HIV, where the virus is completely and permanently eliminated from the body, the ultimate goal.

A cure has proven to be a very tough endeavor. However, there is promise on the horizon. A hopeful avenue of research involves a one-two punch of medication and gene editing. In a recent experiment, scientists first treated HIV-infected mice with a long-acting form of antiretroviral therapy to suppress viral replication. They then snipped out any remaining HIV DNA still lurking in the genomes of the cells by utilizing the CRISPR/Cas9 gene editing system. The result was that no signs of HIV could be detected in more than one-third of the mice.[6]

Even though the mice in this experiment had humanized immune systems, they are not human. More research is needed to figure out how to make this approach to HIV treatment more effective in animal models before researchers can consider moving into clinical trials. With that said, these findings provide a new reason for increased hope that a cure may be found for the millions of people around the world suffering from HIV.

Childhood Cancer Data Initiative (CCDI)

FY 2020 enacted appropriations included $50.0 million for the first year of a planned 10-year initiative in the National Cancer Institute (NCI) to establish a data resource that will aggregate data from pediatric cancer cases and coordinate with partners that maintain data sets on pediatric patients to create a federated, comprehensive, and shared resource to support childhood cancer research in all its forms. The same amount, $50.0 million, is included in the FY 2021 request to support the second year of this initiative. Planning for the initiative included an NCI-hosted symposium last July focusing on opportunities to improve outcomes for children with cancer through enhanced sharing and use of data. Discussions with leaders in the field attending the symposium affirmed the tenets of the initiative. The CCDI plans to build a connected data infrastructure to enable childhood cancer data sharing from multiple sources; to identify opportunities to employ that data better for patients, clinicians, and researchers; and to develop and enhance tools and methods to extract knowledge from the data to directly address challenges in caring for children with cancer. In parallel, NCI has solicited ideas for advancing data sharing for pediatric cancer through an online platform, input from which will inform NCI's efforts to further its investment to collect, analyze, and share data to address the burden of cancer in children, adolescents, and young adults. A public webinar was held in October 2019 to discuss the ideas generated during the July symposium as well as to provide an update on plans for the CCDI.[7]

[5] www.nih.gov/news-events/news-releases/science-clear-hiv-undetectable-equals-untransmittable
[6] www.ncbi.nlm.nih.gov/pubmed/31266936
[7] https://www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative

IDeA States Pediatric Clinical Trials Network (ISPCTN)

The FY 2021 request level continues the annual funding for the ISPCTN in FY 2020 enacted appropriations at $15 million. NIH created the ISPCTN in FY 2016 with up-front funding to address the under-enrollment in clinical trials of children living in rural and medically underserved states. The program leverages the Institutional Development Award (IDeA) program to broaden access to cutting-edge clinical trials, apply findings from other relevant pediatric cohort studies to children in IDeA state locations, and build national pediatric research capacity by providing professional development opportunities for faculty and their support teams as well as supporting investments in infrastructure. Maintaining the annual funding for the ISPCTN in FY 2021 will allow continued support of 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 Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW) pilot studies to develop best practices for treatment of NOW 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.

Artificial Intelligence to Address Chronic Disease

The annual economic impact of chronic diseases is an estimated $3.7 trillion, equivalent to nearly one-fifth of U.S. economic production. NIH proposes an initiative that aims to use Artificial Intelligence (AI) to gain a deeper understanding of the underlying causes of chronic diseases and to identify successful early treatments. The FY 2021 request includes $50.0 million for an initiative that would employ AI, Machine Learning (ML), Deep Learning (DL), and related approaches to enhance the collection, integration, analyses, and interpretation of data related to the onset and progression of chronic diseases. To accomplish these goals, NIH will need to develop new approaches beyond standard grant mechanisms to make existing data AI/ML-ready, support new AI/ML methods, and design new AI/ML-based interventions. The initiative will support new career pathways for investigators who can work at the interface of medicine and computational science and will jumpstart new efforts by articulating bold, scalable problems for the community to engage in through prizes and code-a-thons. The AI/ML effort is in alignment with the HHS-wide AI strategy and in response to the President's February 2019 Executive Order on Maintaining American Leadership in Artificial Intelligence, and also supports the Administration's Industries of the Future initiative.

Tickborne Disease Research

Reported cases of tickborne diseases (TBDs) continue to increase in the United States as tick species expand their geographical reach and new tick-transmitted pathogens emerge. In 2019, NIH published the NIH Strategic Plan for Tickborne Disease Research with five scientific priorities to address the growing threat of TBDs. NIH is committed to implementing this plan by building on existing trans-NIH research efforts to advance fundamental knowledge of TBDs and enable the development of improved diagnostics as well as treatment and prevention strategies. Recent progress in TBD diagnostics includes the newly developed TBD Serochip, which can diagnose up to eight different tick-borne diseases from a single blood sample. Additionally, the

Food and Drug Administration (FDA) recently approved several serological tests for Lyme disease developed by NIH-funded researchers and commercial partners, which has impacted clinical practice with regards to Lyme disease diagnostics. These recently approved tests can now be used in an alternative two-step testing strategy in lieu of the standard two-tier testing algorithm. To improve prevention and treatment strategies, researchers are exploring approaches to develop a vaccine against Lyme disease and are evaluating multiple antibiotics and drug combinations in animal models for activity against Borrelia burgdorferi, the causative agent of Lyme disease. The discovery that a form of red meat allergy can be caused by a tick bite has expanded NIH TBD research to include efforts to better understand the mechanisms regulating the development of this food allergy and the tick and human factors involved in this process. Additionally, researchers are investigating the diagnosis, treatment, and follow-up of Lyme disease patients to assess host and pathogen factors leading to different disease presentations and outcomes of Lyme disease, such as Post Treatment Lyme Disease Syndrome, Lyme arthritis, and encephalopathy. The FY 2021 request level includes an additional $44 million to accelerate NIH's priorities outlined in the Strategic Plan.

Consortium for Innovation in Large-Scale Gene Vector Production

Gene therapy and gene editing approaches are some of the most promising treatment modalities for a growing number of disease conditions. Vectors are the "vehicle" by which a gene can be delivered to a targeted location in the body, and Adeno-Associated Viruses (AAVs) are currently the most prevalent type of vector used in both gene therapy and gene editing studies. Wait times to produce vector therapies that meet the manufacturing standards necessary for clinical trials are long, often one to two years. Resolving this production bottleneck is critical for gene-based therapies to reach all people who need them.

The FY 2021 budget request includes $30.0 million to create a consortium to: 1) establish expanded clinical-grade material production capacity using current methods; 2) develop technologies to increase the efficiency of vector production; 3) design the next generation of vectors with more definable tissue environment or tropism; 4) develop vector methodologies to enable control of their level of expression with an externally applied signal; and 5) avoid use of vectors with complicated and implementation-blocking intellectual property issues. The consortium will focus on providing vectors for academic and government-funded researchers, but standardization and data sharing efforts will produce payoffs for private sector research as well. In the short term, the proposed consortium would plan to fund additional good manufacturing practices (GMP) vector production capacity at existing academic or industry GMP production facilities.

Promoting Influenza Research Innovation

In the United States, the effectiveness of seasonal influenza vaccines, which must be updated each year, ranges from 10 percent to 60 percent. NIH supports a broad research program to improve seasonal influenza vaccines, including through the use of adjuvants that may enhance and broaden protection against diverse influenza strains.

Because different strains of flu respond differently to available drugs, healthcare providers must be able to quickly distinguish one flu strain from another. NIH supports research to design diagnostics that are faster, more accurate, more cost-effective, and more portable. Specifically, NIAID has worked to develop diagnostic platforms capable of examining influenza viruses at the molecular level and rapidly distinguishing flu type A and flu type B as well as the wide variety of subtypes of the type A virus.

Antiviral medicines are an important tool in both controlling influenza by treating the patient's infection and helping to prevent severe illness that can result from flu, including bacterial pneumonia. Because the influenza virus can develop resistance to antiviral drugs, NIAID is working to find new and better treatments to fight the flu. These efforts include supporting the development and testing of the next generation of antiviral drugs. For example, three NIAID clinical trials are currently exploring the effectiveness of novel flu therapeutics in high-risk populations, including human plasma containing high levels of anti-flu antibodies, concentrated human immunoglobulin with high levels of anti-flu antibodies, and a cocktail of the three licensed flu antiviral medicines.

In 2019, NIAID established the Collaborative Influenza Vaccine Innovation Centers, a multidisciplinary program to support research to improve seasonal vaccines and develop promising new influenza vaccine candidates. These activities align with the Executive Order on Modernizing Influenza Vaccines in the United States to Promote National Security and Public Health that was issued on September 19, 2019. The FY 2021 budget maintains the FY 2020 Enacted level for influenza research, including efforts to develop a universal flu vaccine which protects adults and children without the need for a booster.

Improving Research to Save America's Youngest Lives

The Administration wants every child to have the very best chance to live and thrive. In order to help save more pre-mature babies, the Budget prioritizes funding for neonatal research and provides an additional $100 million over 2020 and 2021 dedicated to advancing research and care for America's youngest patients.

Imagining the Future

This is a remarkable time in biomedical research. Truly exciting, world-class science is taking place through NIH support, and leading to breakthroughs in multiple areas as described above. However, there is still much to be done. NIH sees the opportunity for many promising areas of research in the future. Some of the most promising opportunities for transforming human health that the FY 2021 Budget proposes include:

- Enhancing quality of life for those living with diabetes through the development of an artificial pancreas that can automatically sense a person's blood sugar level and adjust insulin dosage precisely.

- Utilizing gene-editing technology to develop a hand-held device capable of detecting gene mutations in minutes, as opposed to weeks, allowing for a quicker start to treatment.

- Improving cancer prognosis through the engineering of nanomedicines that can precisely target cancer cells while limiting toxicity to healthy surrounding cells.

- Pinpointing the mechanism of action of drugs like ketamine, which studies have shown can lift the symptoms of depression within hours instead of weeks.

Conclusion

NIH is at the vanguard of biomedical research, leading the world in support of groundbreaking science. Strategically investing in scientific opportunities such as those described above will help NIH ensure the U.S. remains at the forefront of innovation and discovery. The fruits of NIH research include healthier, longer-living populations as well as substantial economic benefits. Continued, targeted support of NIH is therefore an investment not only in the health and well-being of Americans, but 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 2021 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)[8] 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

[8] https://report.nih.gov/

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 one to three 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.[9, 10] 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, and 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.

[9] The NIH Steering Committee is composed of the NIH Director, Deputy Director (ex-officio), the Directors of the National Cancer Institute, National Heart, Lung, and Blood Institute, and National Institute of Allergy and Infectious Diseases, as well as a balance of Directors from the smaller and medium-sized institutes.

[10] 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]	FY 2019 Final[6]	FY 2020 Enacted[7]	FY 2021 President's Budget	FY 2021 +/- FY 2020
Total, NIH Program Level	**$39,183,862**	**$41,685,000**	**$38,693,631**	**-$2,991,369**
Less mandatory and funds allocated from different sources:				
PHS Program Evaluation	1,146,821	1,230,821	741,000	-489,821
Mandatory Type 1 Diabetes Research - Enacted	150,000	96,575	0	-96,575
Mandatory Type 1 Diabetes Research - Proposed	0	53,425	150,000	96,575
Patient-Centered Outcomes Research Trust Fund	0	0	98,452	98,452
Total, NIH Discretionary Budget Authority	**$37,887,041**	**$40,304,179**	**$37,704,179**	**-$2,600,000**
Interior Budget Authority	79,000	81,000	73,688	-7,312
Total, NIH Labor/HHS Budget Authority	**$37,808,041**	**$40,223,179**	**$37,630,491**	**-$2,592,688**
Number of Competing RPGs[3]	*11,020*	*11,379*	*9,505*	*-1,874*
Total Number of RPGs[3]	*40,667*	*43,027*	*41,607*	*-1,420*
FTE[4]	*17,231*	*18,105*	*18,350*	*245*
NEF[5]	*83,041*	*225,000*	*NA*	*NA*

1 Numbers may not add due to rounding.

2 Includes 21st Century Cures Act funding.

3 Figures for FY 2021 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 2019 and FY 2020 do not include AHRQ.

4 FTE levels include 4 NIH FTEs funded by PHS trust funds in FY 2019 through FY 2021 and 7 FTEs funded by the Patient-Centered Outcomes Research Trust Fund in FY 2021. Figures for FY 2019 and FY 2020 do not include AHRQ.

5 Amounts for FY 2019 reflect notifications submitted to the Committees on Appropriations in the House of Representatives and the Senate on December 4, 2018, and apportioned for use by NIH. Amounts for FY 2020 reflect amounts allocated for NIH from the NEF by sec. 237 of Division A of P.L. 116-94.

6 Excludes hurricane-related supplemental financing.

7 Amounts for FY 2020 reflect directive transfer of $5.0 million from OD to the HHS Office of Inspector General, HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research, and $150.0 million for Type 1 Diabetes Research (enacted amount of $96.575 million through May 22, 2020 plus extension request of $53.425 million).

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	**FY 2020 Enacted**[4]	**FY 2021 President's Budget**[5]	**FY 2021 +/- FY 2020**
Research Project Grants	$23,849.842	$22,089.780	-7.4%
Competing Average Cost (in thousands)	$547.060	$541.278	-1.1%
Number of Competing Awards (whole number)	11,379	9,505	-16.5%
Estimated Competing RPG Success Rate[1]	20.3%	16.5%	-18.7%
Research Centers	$2,663.777	$2,405.752	-9.7%
Other Research	$2,663.482	$2,440.458	-8.4%
Training	$909.923	$847.703	-6.8%
Research & Development Contracts	$3,349.392	$3,077.107	-8.1%
Intramural Research	$4,445.880	$4,076.559	-8.3%
Research Management and Support	$2,014.642	$1,926.132	-4.4%
Common Fund (non-add)	*$639.111*	*$596.467*	*-6.7%*
Buildings & Facilities Appropriation	$200.000	$300.000	50.0%
Other Mechanisms[1]	$1,588.063	$1,431.688	-9.8%
Consolidations (PCORTF)[2]	n/a	$98.452	n/a
Total, Program Level[3]	**$41,685.000**	**$38,693.631**	**-7.2%**

[1] Includes Office of the Director-Other, Buildings and Facilities funding in the National Cancer Institute, and Superfund Research activities funded from the Interior appropriations bill.

[2] Includes mandatory funding from the Patient-Centered Outcomes Research Trust Fund (PCORTF).

[3] Includes discretionary budget authority received from Labor/HHS appropriations bill and the Interior appropriations bill (Superfund). Also includes mandatory budget authority derived from the Type 1 Diabetes account and PCORTF, and Program Evaluation Financing.

[4] Amounts for FY 2020 reflect directive transfer of $5.0 million to the HHS Office of Inspector General and $150.0 million for Type 1 Diabetes Research (enacted amount of $96.575 million through May 22, 2020 plus extension request of $53.425 million).

[5] Includes the proposed consolidation of Agency for Healthcare Research and Quality activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ).

APPROPRIATIONS LANGUAGE

NATIONAL CANCER INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cancer, [$6,245,442,000]*$5,686,173,000*, of which up to $30,000,000 may be used for facilities repairs and improvements at the National Cancer Institute-Frederick Federally Funded Research and Development Center in Frederick, Maryland.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cardiovascular, lung, and blood diseases, and blood and blood products, [$3,624,258,000]*$3,298,004,000*.

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to dental and craniofacial diseases, [$477,429,000]*$434,559,000*.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to diabetes and digestive and kidney disease, [$2,114,314,000]*$1,924,211,000*.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

For carrying out section 301 and title IV of the PHS Act with respect to neurological disorders and stroke, [$2,374,687,000]*$2,195,110,000*.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to allergy and infectious diseases, [$5,885,470,000]*$5,445,886,000*.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to general medical sciences, [$2,937,218,000]*$2,672,074,000*, of which [$1,230,821,000]*$741,000,000* shall be from funds available under section 241 of the PHS Act: *Provided*, That not less than [$386,573,000]*$351,781,000* is provided for the Institutional Development Awards program.

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

For carrying out section 301 and title IV of the PHS Act with respect to child health and human development, [$1,556,879,000]*$1,416,366,000*.

NATIONAL EYE INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, [$824,090,000]*$749,003,000*.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to environmental health sciences, [$802,598,000]*$730,147,000*. (Department of Health and Human Services Appropriations Act, 2020.)

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For necessary expenses for the National Institute of Environmental Health Sciences in carrying out activities set forth in section 311(a) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (42 U.S.C. 9660(a)) and section 126(g) of the Superfund Amendments and Reauthorization Act of 1986, [$81,000,000]*$73,688,000*. (Department of the Interior, Environment, and Related Agencies Appropriations Act, 2020.)

NATIONAL INSTITUTE ON AGING

For carrying out section 301 and title IV of the PHS Act with respect to aging, [$3,543,673,000]*$3,225,782,000*.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to arthritis and musculoskeletal and skin diseases, [$624,889,000]*$568,480,000*.

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

For carrying out section 301 and title IV of the PHS Act with respect to deafness and other communication disorders, [$490,692,000]*$446,397,000*.

NATIONAL INSTITUTE OF NURSING RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to nursing research, [$169,113,000]*$156,804,000*.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

For carrying out section 301 and title IV of the PHS Act with respect to alcohol abuse and alcoholism, [$545,373,000]*$497,346,000*.

NATIONAL INSTITUTE ON DRUG ABUSE

For carrying out section 301 and title IV of the PHS Act with respect to drug abuse, [$1,462,016,000]*$1,431,770,000*.

NATIONAL INSTITUTE OF MENTAL HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to mental health, [$1,968,374,000]*$1,794,865,000*.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to human genome research, [$606,349,000]*$550,116,000*.

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

For carrying out section 301 and title IV of the PHS Act with respect to biomedical imaging and bioengineering research, [$403,638,000]*$368,111,000*.

NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to complementary and integrative health, [$151,740,000]*$138,167,000*.

NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES

For carrying out section 301 and title IV of the PHS Act with respect to minority health and health disparities research, [$335,812,000]*$305,498,000*: *Provided*, That funds may be used to implement a reorganization that is presented to an advisory council in a public meeting and for which the Committees on Appropriations of the House of Representatives and the Senate have been notified 30 days in advance.

JOHN E. FOGARTY INTERNATIONAL CENTER

For carrying out the activities of the John E. Fogarty International Center (described in subpart 2 of part E of title IV of the PHS Act), [$80,760,000]*$73,531,000*.

NATIONAL LIBRARY OF MEDICINE

For carrying out section 301 and title IV of the PHS Act with respect to health information communications, [$456,911,000]*$415,665,000*: *Provided*, That of the amounts available for improvement of information systems, $4,000,000 shall be available until September 30, [2021]*2022*: *Provided further*, That in fiscal year [2020]*2021*, the National Library of Medicine may enter into personal services contracts for the provision of services in facilities owned, operated, or constructed under the jurisdiction of the National Institutes of Health (referred to in this title as "NIH").

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, [$832,888,000]*$787,703,000*: *Provided*, That up to [$60,000,000]*10 percent of the amounts made available under this heading* shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network[: *Provided further*, That at least $578,141,000 is provided to the Clinical and Translational Sciences Awards program].

OFFICE OF THE DIRECTOR

(INCLUDING TRANSFER OF FUNDS)

For carrying out the responsibilities of the Office of the Director, NIH, [$2,239,787,000]*$2,086,463,000*: *Provided*, That funding shall be available for the purchase of not to exceed 29 passenger motor vehicles for replacement only: *Provided further*, That all funds credited to the NIH Management Fund shall remain available for one fiscal year after the fiscal year in which they are deposited: *Provided further*, That [$180,000,000]*$168,763,500* shall be for the Environmental Influences on Child Health Outcomes study: *Provided further*, That [$626,511,000]*$583,867,000* shall be available for the Common Fund established under section 402A(c)(1) of the PHS Act: *Provided further*, That of the funds provided, $10,000 shall be for official reception and representation expenses when specifically approved by the Director of the NIH: *Provided further*, That the Office of AIDS Research within the Office of the Director of the NIH may spend up to $8,000,000 to make grants for construction or renovation of facilities as provided for in section 2354(a)(5)(B) of the PHS Act[: *Provided further*, That $50,000,000 shall be used to carry out section 404I of the PHS Act (42 U.S.C. 283K), relating to biomedical and behavioral research facilities][: *Provided further*, That $5,000,000 shall be transferred to and

merged with the appropriation for the "Office of Inspector General" for oversight of grant programs and operations of the NIH, including agency efforts to ensure the integrity of its grant application evaluation and selection processes, and shall be in addition to funds otherwise made available for oversight of the NIH: *Provided further*, That the funds provided in the previous proviso may be transferred from one specified activity to another with 15 days prior approval of the Committees on Appropriations of the House of Representatives and the Senate: *Provided further*, That the Inspector General shall consult with the Committees on Appropriations of the House of Representatives and the Senate before submitting to the Committees an audit plan for fiscal years 2020 and 2021 no later than 30 days after the date of enactment of this Act]:*Provided further*, That amounts available under this heading are also available to establish, operate, and support the Research Policy Board authorized by section 2034(f) of the 21st Century Cures Act.

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

BUILDINGS AND FACILITIES

For the study of, construction of, demolition of, renovation of, and acquisition of equipment for, facilities of or used by NIH, including the acquisition of real property, [$200,000,000]*$300,000,000*, to remain available through September 30, [2024]*2025*.

NATIONAL INSTITUTE FOR RESEARCH ON SAFETY AND QUALITY

For carrying out titles III and IX of the PHS Act, part A of title XI of the Social Security Act, and section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, $256,660,000: Provided, That section 947(c) of the PHS Act shall not apply in fiscal year 2021: Provided further, That in addition, amounts received from Freedom of Information Act fees, reimbursable and interagency agreements, and the sale of data shall be credited to this appropriation and shall remain available until expended.

NIH INNOVATION ACCOUNT, CURES ACT

(INCLUDING TRANSFER OF FUNDS)

For necessary expenses to carry out the purposes described in section 1001(b)(4) of the 21st Century Cures Act, in addition to amounts available for such purposes in the appropriations provided to the NIH in this Act, **[**$492,000,000**]***$404,000,000*, to remain available until expended: *Provided*, That such amounts are appropriated pursuant to section 1001(b)(3) of such Act, are to be derived from amounts transferred under section 1001(b)(2)(A) of such Act, and may be transferred by the Director of the National Institutes of Health to other accounts of the National Institutes of Health solely for the purposes provided in such Act: *Provided further*, That upon a determination by the Director that funds transferred pursuant to the previous proviso are not necessary for the purposes provided, such amounts may be transferred back to the Account: *Provided further*, That the transfer authority provided under this heading is in addition to any other transfer authority provided by law. (Department of Health and Human Services Appropriations Act, 2020.)

LANGUAGE ANALYSIS

Language Provision to be Changed	Explanation/Justification
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES *Provided*, That up to [$60,000,000]*10 percent of the amounts made available under this heading* shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network	The unique authorities associated with the Cures Acceleration Network (CAN) – use of Other Transactions Authority (OTA) and matching funding – give NCATS flexibility to quickly create or terminate parts of an initiative based on programmatic need and scientific priority. Specifying the CAN ceiling as a percentage of the overall NCATS budget ensures that CAN funding adjusts relative to overall funding levels and enables NCATS to plan CAN activities more strategically.
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES [: *Provided further*, That at least $578,141,000 is provided to the Clinical and Translational Sciences Awards program].	This removal would give NCATS flexibility in the amounts allocated to the Clinical and Translational Sciences Awards program in order to preserve flexibility in managing its budget within the President's Budget request level.
OFFICE OF THE DIRECTOR [: *Provided further*, That $50,000,000 shall be used to carry out section 404I of the PHS Act (42 U.S.C. 283K), relating to biomedical and behavioral research facilities]	The FY 2021 President's Budget does not request continued funding for the construction and renovation of extramural research facilities.

Language Provision to be Changed	Explanation/Justification
OFFICE OF THE DIRECTOR [: *Provided further*, That $5,000,000 shall be transferred to and merged with the appropriation for the "Office of Inspector General" for oversight of grant programs and operations of the NIH, including agency efforts to ensure the integrity of its grant application evaluation and selection processes, and shall be in addition to funds otherwise made available for oversight of the NIH: *Provided further*, That the funds provided in the previous proviso may be transferred from one specified activity to another with 15 days prior approval of the Committees on Appropriations of the House of Representatives and the Senate: *Provided further*, That the Inspector General shall consult with the Committees on Appropriations of the House of Representatives and the Senate before submitting to the Committees an audit plan for fiscal years 2020 and 2021 no later than 30 days after the date of enactment of this Act]	The FY 2021 President's Budget does not request funds for NIH to transfer to the Office of Inspector General (OIG). Funding for the OIG is provided directly in the OIG appropriation.

BUDGET MECHANISM TABLE

Budget Mechanism - Total[1,2,3]

(Dollars in Thousands)[1,2,3]	FY 2019 Final[4]		FY 2020 Enacted[5]		FY 2021 President's Budget[6]		FY 2021 +/- FY 2020	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	27,624	$14,564,519	29,508	$16,004,065	30,109	$15,631,587	601	-$372,478
Administrative Supplements[3]	*(2,341)*	437,486	*(2,300)*	501,907	*(1,517)*	277,780	*(-783)*	-224,127
Competing	11,020	$6,313,647	11,379	$6,224,996	9,505	$5,144,843	-1,874	-$1,080,153
Subtotal, RPGs	38,644	$21,315,652	40,887	$22,730,968	39,614	$21,054,209	-1,273	-$1,676,758
SBIR/STTR	2,023	1,052,394	2,140	1,118,874	1,993	1,035,570	-147	-83,304
Research Project Grants	40,667	$22,368,046	43,027	$23,849,842	41,607	$22,089,780	-1,420	-$1,760,062
Research Centers:								
Specialized/Comprehensive	998	$1,927,569	1,021	$1,895,832	926	$1,693,289	-95	-$202,542
Clinical Research	70	420,992	67	427,137	66	397,046	-1	-30,091
Biotechnology	85	142,465	79	134,917	75	122,935	-4	-11,982
Comparative Medicine	50	136,741	49	131,392	47	124,233	-2	-7,159
Research Centers in Minority Institutions	19	63,189	21	74,500	21	68,250	0	-6,250
Research Centers	1,222	$2,690,957	1,237	$2,663,777	1,135	$2,405,752	-102	-$258,024
Other Research:								
Research Careers	4,222	$790,182	4,445	$824,556	4,168	$773,975	-277	-$50,581
Cancer Education	77	20,459	101	26,890	96	25,546	-5	-1,345
Cooperative Clinical Research	257	468,112	277	461,252	232	398,865	-45	-62,387
Biomedical Research Support	131	81,134	128	80,408	119	74,706	-9	-5,702
Minority Biomedical Research Support	286	100,758	280	98,477	240	84,534	-40	-13,943
Other	2,134	1,113,725	2,277	1,171,899	2,159	1,082,833	-118	-89,066
Other Research	7,107	$2,574,370	7,508	$2,663,482	7,014	$2,440,458	-494	-$223,024
Total Research Grants	48,996	$27,633,373	51,772	$29,177,100	49,756	$26,935,990	-2,016	-$2,241,110
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,654	$170,240	3,814	$183,810	3,598	$172,660	-216	-$11,151
Institutional Awards	13,221	695,065	13,833	726,112	12,707	675,043	-1,126	-51,069
Total Research Training	16,875	$865,305	17,647	$909,923	16,305	$847,703	-1,342	-$62,220
Research & Develop. Contracts	2,455	$3,164,921	2,663	$3,349,392	2,409	$3,077,107	-254	-$272,285
(SBIR/STTR) (non-add)[3]	*(129)*	*(91,059)*	*(113)*	*(81,196)*	*(103)*	*(74,359)*	*(-10)*	*(-6,836)*
Intramural Research		$4,143,842		$4,445,880		$4,076,559		-$369,321
Res. Management & Support		1,883,396		2,014,642		1,926,132		-88,510
Res. Management & Support (SBIR Admin) (non-add)[3]		*(8,175)*		*(11,219)*		*(8,426)*		*(-2,793)*
Office of the Director - Appropriation[3,7]		*(2,103,986)*		*(2,404,387)*		*(2,208,063)*		*(-196,324)*
Office of the Director - Other		1,196,712		1,477,063		1,343,000		-134,063
ORIP (non-add)[3,7]		*(288,108)*		*(288,213)*		*(268,596)*		*(-19,617)*
Common Fund (non-add)[3,7]		*(619,166)*		*(639,111)*		*(596,467)*		*(-42,644)*
Buildings and Facilities[8]		217,313		230,000		315,000		85,000
Appropriation[3]		*(199,313)*		*(200,000)*		*(300,000)*		*(100,000)*
Type 1 Diabetes[9,10]		-150,000		-150,000		-150,000		0
Program Evaluation Financing[9]		-1,146,821		-1,230,821		-741,000		489,821
Subtotal, Labor/HHS Budget Authority		**$37,808,041**		**$40,223,179**		**$37,630,491**		**-$2,592,688**
Interior Appropriation for Superfund Research		79,000		81,000		73,688		-7,312
Total, NIH Discretionary Budget Authority		**$37,887,041**		**$40,304,179**		**$37,704,179**		**-$2,600,000**
Type 1 Diabetes[10]		150,000		150,000		150,000		0
Patient-Centered Outcomes Research Trust Fund (PCORTF)		0		0		98,452		98,452
Total, NIH Budget Authority		**$38,037,041**		**$40,454,179**		**$37,952,631**		**-$2,501,548**
Program Evaluation Financing		1,146,821		1,230,821		741,000		-489,821
Total, Program Level		**$39,183,862**		**$41,685,000**		**$38,693,631**		**-$2,991,369**

1 All Subtotal and Total numbers may not add due to rounding.
2 Includes 21st Century Cures Act funding and excludes hurricane-related supplemental financing.
3 All numbers in italics and brackets are non-add.
4 Includes $186.4 million of 21st Century Cures and $76.5 million of Type 1 Diabetes funding appropriated in FY 2019 and carried over into FY 2020. Numbers of grants and dollars for carryover are distributed by mechanism.
5 Reflects transfer of $5.0 million to the HHS OIG.
6 Includes the proposed consolidation of Agency for Healthcare Research and Quality activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ), distributed by mechanism.
7 Number of grants and dollars for the Common Fund and ORIP components of OD are distributed by mechanism and are noted here as non-adds. Office of the Director - Appropriation is the non-add total of these amounts and the funds accounted for under OD - Other.
8 Includes B&F appropriation and monies allocated ($18.0 million in FY 2019, $30.0 million in FY 2020, and $15.0 million in FY 2021) pursuant to appropriations acts provisions that funding may be used for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
9 Number of grants and dollars for mandatory Type 1 Diabetes (T1D) and NIGMS Program Evaluation financing are distributed by mechanism above; therefore, T1D and Program Evaluation financing amounts are deducted to provide subtotals for Labor/HHS Budget Authority.
10 FY 2020 reflects requested extension of Type 1 Diabetes Research from enacted amount of $96.575 million through May 22, 2020 to full-year level of $150.0 million.

AUTHORIZING LEGISLATION

(Dollars in Thousands)	FY 2020 Amount Authorized	FY 2020 Amount Appropriated[1]	FY 2021 Amount Authorized	FY 2021 President's Budget
National Institutes of Health Activity:				
1. Biomedical Research under Section 301 and title IV of the PHS Act:				
General Authorization: Section 402A(a)(1) of the PHS Act	36,472,443	40,954,400	TBD	37,698,231
Pediatric Research Initiative: Section 402A(a)(2) of the PHS Act	12,600	12,600	12,600	12,600
2. Superfund Research Program: Section 311(a) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, and Section 126(g) of the Superfund Amendments and Reauthorization Act of 1986	Indefinite	81,000	Indefinite	73,688
3. 21st Century Cures Act:				
Precision Medicine: Section 1001(b)(4)(A)	149,000	149,000	109,000	109,000
BRAIN Initiative: Section 1001(b)(4)(B)	140,000	140,000	100,000	100,000
Cancer Moonshot: Section 1001(b)(4)(C)	195,000	195,000	195,000	195,000
Regenerative Medicine: Section 1001(b)(4)(D)	8,000	8,000	0	0
4. Special Diabetes Programs: Section 330B(b) of the PHS Act	96,575	96,575	TBD	150,000
5. Research on Healthcare and Quality: Titles III and Title IX and Section 947(c) of the PHS Act, as amended	SSAN	338,000	SSAN	256,660

[1]The amount appropriated in FY 2020 for the Special Diabetes Programs reflects the extended funding level for Oct 1, 2019 to May 22, 2020.

SSAN = Such sums as necessary

APPROPRIATIONS HISTORY

Fiscal Year	Budget Request to Congress	House Allowance	Senate Allowance	Appropriation [1]
FY 2012	$31,979,000,000		$30,630,423,000	$30,852,187,000 [2]
FY 2013				
Base	$30,852,187,000		$30,810,387,000	$30,929,977,000 [3]
Sequestration				-1,552,593,211
Subtotal	$30,852,187,000		$30,810,387,000	$29,377,383,789
FY 2014	$31,323,187,000		$31,176,187,000	$30,142,653,000
FY 2015	$30,353,453,000		$30,084,304,000	$30,311,349,000 [4]
FY 2016	$31,311,349,000 [5]	$31,411,349,000	$32,311,349,000	$32,311,349,000 [6]
FY 2017	$33,136,349,000 [7]	$33,463,438,000	$34,311,349,000	$34,229,139,000 [8]
FY 2018	$26,919,710,000 [9]	$35,184,000,000	$36,084,000,000	$37,311,349,000 [10]
FY 2019	$34,766,707,000 [11]	$38,564,000,000	$39,312,349,000	$39,313,000,000 [12]
FY 2020	$34,111,669,000 [11]	$41,154,000,000	$42,084,000,000	$41,636,575,000 [13]
FY 2021 PB	$38,693,631,000 [11,14]			

[1] Does not reflect comparability adjustments. Interior appropriation's Superfund Research allocation included for all years. Special Type 1 Diabetes Research mandatory funding included. Includes CURES amounts of $352,000,000 in FY 2017, $496,000,000 in FY 2018, $711,000,000 in FY 2019, $492,000,000 in FY 2020, and $404,000,000 in the FY 2021 Request.

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

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

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

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

[6] Includes Program Evaluation Financing of $780,000,000. Excludes Ebola-related and Zika-related funding.

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

[8] Includes Program Evaluation Financing of $824,443,000.

[9] Includes Program Evaluation Financing of $780,000,000.

[10] Includes Program Evaluation Financing of $922,871,000. Excludes supplemental hurricane funding of $50,000,000 to the Office of the Director for extramural construction.

[11] Includes Program Evaluation Financing of $741,000,000.

[12] Includes Program Evaluation Financing of $1,146,821,000. Does not reflect $5,000,000 transfer from NIH to the HHS Office of the Inspector General or hurricane disaster supplemental of $1,000,000 for National Institute of Environment Health Sciences.

[13] Includes Program Evaluation Financing of $1,230,821,000. Does not reflect $5,000,000 transfer from NIH to HHS Office of the Inspector General.

[14] Includes funding of $355,112,000 for the National Institute for Research on Safety and Quality (NIRSQ) associated with the proposed FY 2021 consolidation into NIH. Figures prior to FY 2021 do not include amounts for the Agency for Healthcare Research and Quality (AHRQ). For information on AHRQ Funding History, see the NIRSQ chapter of the NIH Congressional Justification.

NARRATIVE BY ACTIVITY TABLE/HEADER TABLE

(Dollars in Thousands)	FY 2019 Final [1]	FY 2020 Enacted [2]	FY 2021 President's Budget	FY 2021 +/- FY 2020
Program Level [3,4]	$39,183,862	$41,685,000	$38,693,631	-2,991,369
FTE [3,5]	17,231	18,105	18,350	245

[1] Excludes hurricane-related supplemental financing.

[2] Amount for FY 2020 reflects directive transfer of $5.0 million to the HHS Office of Inspector General and requested extension of Type 1 Diabetes Research from enacted amount of $96.575 million through May 22, 2020 to full-year level of $150.0 million.

[3] Figures for FY 2021 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 2019 and FY 2020 do not include AHRQ.

[4] Includes 21st Century Cures Act funding, Mandatory Type 1 Diabetes, and Superfund in all years; includes NIGMS Program Evaluation funding of $1,146.8 million in FY 2019, $1,230.8 million in FY 2020, and $741.0 million in FY 2021.

[5] Represents NIH target FTE level, including direct funded and reimbursable funded FTE.

Authorizing Legislation: For existing NIH program, Section 301 and Title IV of the Public Health Act, as amended. For NIRSQ, Title III and Title IX and Section 947(c) of the Public Health Service Act, as amended, and Section 1013 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.

Allocation Methods: Competitive Grants; Contract; Intramural; Other

PROGRAM DESCRIPTIONS AND ACCOMPLISHMENTS

NIH Contributions and Scientific Advances Towards Improving Human Health

NIH is the largest public funder of biomedical research in the world, investing taxpayer dollars wisely to achieve its mission to enhance health, lengthen life, and reduce illness and disability. In pursuing this mission, NIH improves health by promoting treatment and prevention, contributes to society by driving economic growth and productivity, and expands the biomedical knowledge base by funding cutting-edge research and cultivating the biomedical workforce of today and tomorrow.

NIH-funded scientists report thousands of new findings every year across the spectrum of biomedical science, from basic, translational, and clinical research studies. A few recent NIH-funded research accomplishments are listed below.

AI Approach Outperformed Human Experts in Identifying Cervical Precancer

A research team led by investigators from NIH and Global Good developed a computer algorithm that can analyze digital images of a woman's cervix and accurately identify precancerous changes that require medical attention.[11] This artificial intelligence (AI) approach, called automated visual evaluation, has the potential to revolutionize cervical cancer screening, particularly in low-resource settings.

Researchers used comprehensive datasets to "train" a learning algorithm to recognize patterns in complex visual inputs, such as medical images.[12] To create the algorithm, the research team used more than 60,000 cervical images from a National Cancer Institute (NCI) archive of photos collected during a cervical cancer screening study that was carried out in Costa Rica in the 1990s. More than 9,400 women participated in that population study, with follow-up that lasted up to 18 years. Because of the prospective nature of the study, the researchers gained nearly complete information on which cervical changes became precancers and which did not. The findings were then subsequently confirmed independently by experts at the National Library of Medicine (NLM).

The researchers plan to further train the algorithm on a sample of representative images of cervical precancers and normal cervical tissue from women in communities around the world, using a variety of cameras and other imaging options. The ultimate goal of the project is to create the best possible algorithm for common, open use.

Curing Sickle Cell Disease

In large part due to the advances made through NIH-supported research, many patients with Sickle Cell Disease (SCD) now can expect to live between 55-65 years of age.[13] As recently as

[11] www.nih.gov/news-events/news-releases/ai-approach-outperformed-human-experts-identifying-cervical-precancer
[12] Hu L. et al. *J Natl Cancer Inst*. 2019 Sep;111(9):923-932. doi: 10.1093/jnci/djy225. PMID:30629194
[13] magazine.medlineplus.gov/article/is-a-widely-available-cure-for-sickle-cell-disease-on-the-horizon

the 1970s, the average person with SCD died in childhood, mainly from infection. Children suffering from SCD were also especially vulnerable to suffering fatal or debilitating strokes. NIH-supported research discovered that a daily dose of penicillin could prevent life-threatening infections in infants with SCD, thus establishing a new standard of care and providing an impetus for now universal newborn screening in the United States.[14] Research has also found ways to identify children with SCD who are at high risk for stroke. As a result, the risk of childhood stroke has been reduced by 90 percent.

The future for those with SCD has never been more promising, as there are a variety of new and innovative strategies being explored to cure this devastating disease. One particularly promising avenue of research involves using gene editing techniques. Shortly after birth, babies usually stop producing fetal hemoglobin and switch over to the adult form. However, rare individuals continue to produce high levels of fetal hemoglobin throughout their lives. Studies have shown that individuals with SCD who continue producing fetal hemoglobin have an extremely mild version of the disease—essentially the presence of significant quantities of fetal hemoglobin provides protection against SCD. Researchers are now exploring ways to boost the fetal hemoglobin levels in everyone with SCD, and gene editing may provide an effective, long-lasting way to do this.[15]

Based on this and other approaches currently being tested, it appears that we are within sight of curing sickle cell disease. Even more exciting, if a cure for SCD is finally realized, a similar strategy could be applied to other genetic conditions that currently lack any effective treatment.

Scientists Translate Brain Signals into Speech Sounds

Scientists used brain signals recorded from epilepsy patients to program a computer to mimic natural speech — an advancement that could one day have a profound effect on the ability of certain patients to communicate. Speech scientists and neurologists from the University of California, San Francisco recreated many vocal sounds with varying accuracy using brain signals recorded from epilepsy patients with normal speaking abilities.[16] The patients were asked to speak full sentences, and the data obtained from brain scans was then used to drive computer-generated speech. Furthermore, simply miming the act of speaking provided sufficient information to the computer for it to recreate several of the same sounds.

The loss of the ability to speak can have devastating effects on patients whose facial, tongue, and larynx muscles have been paralyzed due to stroke or other neurological conditions. Technology has helped these patients to communicate through devices that translate head or eye movements into speech. Because these systems involve the selection of individual letters or whole words to build sentences, the speed at which they can operate is very limited. Instead of recreating sounds based on individual letters or words, the goal of this project was to synthesize the specific sounds used in natural speech.

[14] archives.nih.gov/asites/report/09-09-2019/report.nih.gov/nihfactsheets/ViewFactSheet2ad4.html?csid=116
[15] directorsblog.nih.gov/tag/fetal-hemoglobin/
[16] Anumanchipalli, G.K. *Nature*. 2019 Apr; 568(7753):493-498. doi: 10.1038/s41586-019-1119-1. PMID: 31019317.

Scientists first recorded signals from patients' brains while they were asked to speak or mime sentences and then built maps of how the brain directs the vocal tract, including the lips, tongue, jaw, and vocal cords, to make different sounds. The researchers then applied those maps to a computer program that produced synthetic speech. Volunteers were asked to listen to the synthesized sentences and to transcribe what they heard. More than half the time, the listeners were able to determine the sentences being spoken by the computer correctly.

The researchers' next plan is to design a clinical trial involving paralyzed, speech-impaired patients to determine how best to gather brain signal data that can then be applied to the previously trained computer algorithm.

Study Funded by NIH Supports Optimal Threshold for Diagnosing COPD

An NIH-funded study provides evidence to support a simple measurement for diagnosing clinically significant airflow obstruction, the key characteristic of chronic obstructive pulmonary disease (COPD), the fourth leading cause of death in the United States.[17] The study found that a 70 percent ratio of two indicators of lung function proved as accurate as or more accurate than other thresholds for predicting COPD-related hospitalizations and deaths.

The research, which draws on a wide range of multi-ethnic studies, validates current guidelines from major respiratory societies and contributes to identify a fixed threshold of disease severity. This approach has led to great strides in early detection and treatment of other conditions such as hypertension and diabetes.

The researchers aimed to determine how accurate various thresholds were in predicting COPD-related hospitalizations and mortality. For that, the NHLBI Pooled Cohorts Study analyzed data from four U.S. population-based studies that collected spirometry results and followed up participants for COPD-related clinical events. The study included 24,207 adult participants, of whom 54 percent were women, 69 percent white, and 24 percent black.

Establishing a diagnostic threshold may result in earlier detection and treatment options for patients.

Brain Biomarkers Could Help Identify Those at Risk for PTSD

A study has shed light on the neurocomputational contributions to the development of post-traumatic stress disorder (PTSD) in combat veterans.[18] The findings revealed distinct patterns for how the brain and body respond to learning danger and safety, depending on the severity of PTSD symptoms. These findings could help explain why symptoms of PTSD can be severe for some people but not others.

One theory explaining why some symptoms of PTSD develop suggests that during a traumatic event, a person may learn to view the people, locations, and objects that are present as being

[17] Bhatt, S.P. et al. *JAMA*. 2019 Jun; 321(24): 2438–2447. doi: 10.1001/jama.2019.7233 PMCID: PMC6593636
[18] Homan, Philipp, et al. *Nat Neurosci*. 2019 Mar; 22(3): 470–476. P. doi: 10.1038/s41593-018-0315-x PMCID: PMC6829910

dangerous if they become associated with the threatening situation. While some of these things may be dangerous, some are safe. PTSD symptoms result when these safe stimuli continue to trigger fearful and defensive responses long after the trauma has occurred. Despite the prominence of this theory, the way in which this learning occurs is not well understood.

Researchers at Yale University and Mount Sinai examined how the mental adjustments performed during learning and the way in which the brain tracks these adjustments relate to PTSD symptom severity. Although all participants, regardless of PTSD symptomology, were able to perform a reversal learning exercise, when the researchers took a closer look at the data, they found highly symptomatic veterans responded with greater corrections in their physiological arousal and several brain regions to cues that did not predict what they had expected.

These results show that PTSD symptom severity is reflected in how combat veterans respond to negative surprises in the environment—when outcomes predicted by cues are not as expected—and the way in which the brain is attuned to these stimuli is different. These findings will allow for a more fine-grained understanding of how learning processes may go awry in the aftermath of combat trauma and provide more specific targets for treatment.

Data Sharing Uncovers Five New Risk Genes for Alzheimer's Disease

An international study involving the analysis of genetic data from more than 94,000 individuals revealed 5 new risk genes for Alzheimer's disease and confirmed 20 known others.[19] The researchers also reported for the first time that mutations in genes specific to tau, a hallmark protein of Alzheimer's disease, may play an earlier role in the development of the disease than originally thought. These new findings support developing evidence that groups of genes associated with specific biological processes, such as cell trafficking, lipid transport, inflammation, and the immune response, are "genetic hubs" that are an important part of the disease process.

In addition to confirming the known association of 20 genes with risk of Alzheimer's and identifying 5 additional Alzheimer's-associated genes, these genes were analyzed to see what cellular pathways might be implicated in the disease process. The pathway analysis implicated the immune system, lipid metabolism, and amyloid precursor protein (APP) metabolism. Mutations in the APP gene have been shown to be directly related to early onset Alzheimer's. The present study, done in late onset Alzheimer's subjects, suggests that variants affecting APP and amyloid beta protein processing are associated with both early-onset autosomal dominant Alzheimer's and with late onset Alzheimer's**.** In addition, for the first time, the study implicated a genetic link to tau binding proteins. Taken together, data suggest that therapies developed by studying subjects with early-onset disease could also be applied to the late-onset form of Alzheimer's.

Once the functions of the 5 genes newly associated with Alzheimer's are understood and examined in conjunction with the functions of the 20 known genes, researchers will be in a better position to identify where the genetic hubs of Alzheimer's are clustering. Armed with these

[19] Kunkle BW et al. *Nature Genetics*. 2019 Feb; 51:414-430. doi: 10.1038/s41588-019-0358-2

findings, researchers can look more deeply into these genetic hubs to reveal disease mechanisms and potential drug targets.

Scientists Find New Approach That Shows Promise for Treating Cystic Fibrosis

Researchers have discovered that a widely used antifungal drug may hold promise for treating people with cystic fibrosis, a life-threatening genetic disorder that causes serious damage to the lungs.[20] In studies using human cells and animal models, the researchers found that the drug, called amphotericin, helps lung cells function in a way that could make it easier for patients to fight chronic bacterial lung infections that are a hallmark of the disease.

If subsequent human studies validate the findings, the use of the drug could be good news to the more than 30,000 people in the United States and 70,000 worldwide who live with cystic fibrosis, a disease with no cure and few treatment options. It holds special promise for a subset of patients, about 10 percent of the people with cystic fibrosis, who do not respond to any treatment.

In their studies, the researchers used lung tissue from patients with cystic fibrosis, as well as pig models of cystic fibrosis, and found that amphotericin spurred a host of changes associated with improved lung function — restoration of pH levels, improved viscosity, and increased antibacterial activity, among others.

The researchers noted that amphotericin can be delivered directly to the lungs to avoid common side effects. More experimental studies are needed before the drug is safe to treat cystic fibrosis in people, but experts are hopeful.

Gene Therapy Restores Immunity in Infants with Rare Immunodeficiency Disease

A small clinical trial has shown that gene therapy can safely correct the immune systems of infants newly diagnosed with a rare, life-threatening inherited disorder in which infection-fighting immune cells do not develop or function normally. Eight infants with the disorder, called X-linked severe combined immunodeficiency (X-SCID), received an experimental gene therapy co-developed by NIH scientists.[21] They experienced substantial improvements in immune system function and were growing normally up to two years after treatment. The new approach appears safer and more effective than previously tested gene-therapy strategies for X-SCID.

Infants with X-SCID, caused by a gene mutation, are highly susceptible to severe infections. If untreated, the disease is fatal, usually within the first year or two of life.[22] Infants with X-SCID typically are treated with transplants of blood-forming stem cells, ideally from a genetically matched sibling. However, less than 20 percent of infants with the disease have such a donor.

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[20] Muraglia, KA et al. *Nature*. 2019 Mar; 567(7748): 405–408. doi: 10.1038/s41586-019-1018-5 PMCID: PMC6492938

[21] Mamcarz, E et al. *N Engl J Med.* 2019 Apr; 380(16): 1525-1534. doi: 10.1056/NEJMoa1815408 PMCID: PMC6636624

[22] www.nih.gov/news-events/news-releases/gene-therapy-restores-immunity-infants-rare-immunodeficiency-disease

Those without a matched sibling typically receive transplants from a parent or other donor, which are lifesaving, but often only partially restore immunity. These patients require lifelong treatment and may continue to experience complex medical problems, including chronic infections.

To restore immune function to those with X-SCID, scientists developed an experimental gene therapy that involves inserting a normal copy of the mutated gene into the patient's own blood-forming stem cells. Compared with previously tested gene-therapy strategies for X-SCID, which used other vectors and chemotherapy regimens, the current approach appears safer and more effective. Researchers are continuing to monitor the infants who received the lentiviral gene therapy to evaluate the durability of immune reconstitution and assess any potential long-term side effects of the treatment.

Emergency Treatment Guidelines Improve Survival of People with Severe Head Injury

A large study of more than 21,000 people finds that training emergency medical services (EMS) agencies to implement prehospital guidelines for traumatic brain injury (TBI) may help improve survival in patients with severe head trauma.[23]

Based on observational studies, guidelines for prehospital management of TBI that were developed in 2000, and updated in 2007, focused on preventing low oxygen, low blood pressure, and hyperventilation in people with head injury. Collectively, the studies suggested that controlling those factors before patients arrived at the hospital could improve survival, but actual adherence to the guidelines had not been examined.

Researchers compared patient outcomes before and after the guideline implementation. All patients in the study experienced head injury with loss of consciousness. The results revealed that the guidelines helped double the survival rate of people with severe TBI and triple the survival rate in severe TBI patients who had to have a breathing tube inserted by EMS personnel. The guidelines were also associated with an overall increase in survival to hospital admission.

Although the guidelines provide specific recommendations for oxygen levels and blood pressure, researchers will examine whether those ranges should be revised. More research is needed to determine the best strategies for airway management and breathing support to optimize ventilation. Additional studies will investigate the best methods for national and global adoption of the TBI guidelines.

Human Antibody Reveals Hidden Vulnerability in Influenza Virus

Scientists have discovered that the "head" of an influenza virus protein has an unexpected Achilles heel. The team discovered and characterized the structure of a naturally occurring human antibody that recognizes and disrupts a portion of the hemagglutinin (HA) protein that the virus uses to enter and infect cells. The investigators determined that the antibody, FluA-20,

[23] Spaite DW.. et al., *Acad Emerg Med.* 2014 Jul;21(7):818-30. doi: 10.1111/acem.12411. PMCID: PMC4134700

binds tightly to an area on the globular head of the HA protein that is only very briefly accessible to antibody attack.[24] The site was not expected to be vulnerable to such a strike.

The researchers isolated the FluA-20 antibody from a person who had received many influenza immunizations. In a series of experiments, they showed that FluA-20 can "reach into" an otherwise inaccessible part of the HA molecule and cause it to fall apart, thus preventing the spread of the virus from cell to cell. This discovery came as a surprise because this region of HA was thought to be stable and inaccessible to antibodies.

In mouse studies, FluA-20 prevented infection or illness when the animals were exposed to four different influenza A viral subtypes that cause disease in humans. Two viruses used in the experiments are Group 1 influenza subtypes, while the two others are members of Group 2. Current influenza vaccines must contain viral components from both subtypes to elicit matching antibodies. A single vaccine able to generate potent antibodies against members of both groups could provide broad multi-year protection against influenza.

Blood Test Shows Promise for Early Detection of Severe Lung-Transplant Rejection

Researchers have developed a simple blood test that can detect when a newly transplanted lung is being rejected by a patient, even when no outward signs of the rejection are evident.[25] The test could make it possible for doctors to intervene faster to prevent or slow down so-called chronic rejection—which is severe, irreversible, and often deadly—in those first critical months after lung transplantation. Researchers believe this same test might also be useful for monitoring rejection in other types of organ transplants.

The test relies on DNA sequencing, and as such, represents a great example of personalized medicine, as it will allow doctors to tailor transplant treatments to those individuals who are at highest risk for rejection. Lung transplant recipients have the shortest survival rates among patients who get solid organ transplantation of any kind—only about half live past five years. Lung transplant recipients face a high incidence of chronic rejection, which occurs when the body's immune system attacks the transplanted organ. Existing tools for detecting signs of rejection, such as biopsy, either require the removal of small amounts of lung tissue or are not sensitive enough to discern the severity of the rejection. The new test appears to overcome those challenges.

If validated, this blood test could become a routine tool used to monitor transplant patients at very early stages of rejection, the researchers said.

New Protocol Could Ease Diagnosis of Bacterial Infections in Infants

A new protocol could help emergency room physicians to rule out life-threatening bacterial infections among infants up to two months of age who have fevers, potentially eliminating the

[24] Bangaru S. et al. *Cell*. 2019 May ;177(5):1136-1152. doi: 10.1016/j.cell.2019.04.011 PMCID:PMC6629437
[25] Agbor-Enoh, S. et al. *EBioMedicine*. 2019 Feb; 40: 541–553. doi: 10.1016/j.ebiom.2018.12.029 PMCID: PMC6412014

need for spinal taps, unnecessary antibiotic treatments or expensive hospital stays[26]. Researchers from the Pediatric Emergency Care Applied Research Network (PECARN) developed the protocol from a study of more than 1,800 infants seen at 26 emergency departments around the country.

Previous studies suggest that 8 to 13 percent of infants up to 2 months of age who have a fever may have a serious bacterial infection. These include urinary tract infections, bacteremia, and bacterial meningitis. Often, a physician will need to confirm a diagnosis with a spinal tap, in which a small amount of fluid is extracted from the spinal canal. Although complications of the procedure are rare, they include inflammation of the spinal canal, bleeding and headache. In addition, an infant may be given antibiotics when a bacterial infection is suspected and may be admitted to a hospital for observation.

The new protocol measures the levels of bacteria in urine, of procalcitonin (a substance produced in response to bacterial infection) in serum, and of neutrophils (an infection-fighting white blood cell). The researchers ruled out a serious bacterial infection (SBI) if tests showed low levels of bacteria and procalcitonin and a normal neutrophil count. They were able to rule out accurately all but 3 of the 170 cases of SBI ultimately detected, including all cases of meningitis.

NIH Establishes Network to Improve Opioid Addiction Treatment in Criminal Justice Settings

NIH awarded 15 grants to form the Justice Community Opioid Innovation Network (JCOIN) to support research on quality addiction treatment for opioid use disorder (OUD) in criminal justice settings nationwide.[27] The awards total an estimated $141.3 million from the National Institute on Drug Abuse (NIDA).

JCOIN will establish a national network of investigators collaborating with justice and behavioral health stakeholders to research promising interventions and other approaches to improve the capacity of the justice system to respond to the opioid crisis.[28] JCOIN is part of the NIH Helping to End Addiction Long-term (HEAL) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. The NIH HEAL Initiative is focused on improving prevention and treatment strategies for opioid misuse and addiction and enhancing pain management.

Awarded research centers will study evidence-based medications, behavioral interventions, digital therapeutics, and comprehensive patient-centered treatments in 15 states and Puerto Rico. Each grantee will work with five or more communities, where they will engage with organizations in justice settings and service providers in the community. JCOIN will address gaps in OUD treatment and related services in a wide range of criminal justice settings, including jails, drug courts, problem-solving courts, policing and diversion, re-entry, and probation and parole.

[26] Kuppermann, N. *JAMA pediatrics*. 2019 Feb, 173(4): 342. DOI: 10.1001/jamapediatrics.2018.5501
[27] heal.nih.gov/research/research-to-practice/jcoin
[28] www.nih.gov/news-events/news-releases/nih-establishes-network-improve-opioid-addiction-treatment-criminal-justice-settings

Drug Delays Type 1 Diabetes in People at High Risk

Researchers showed that a treatment affecting the immune system has effectively slowed the progression to clinical type 1 diabetes in high-risk individuals.[29] The study is the first to show that clinical type 1 diabetes can be delayed by two or more years among people who are at high risk.

The international study involved treatment with an anti-CD3 monoclonal antibody (teplizumab) aimed at discovering ways to delay or prevent type 1 diabetes. Researchers enrolled 76 participants ages 8-49 who were relatives of people with type 1 diabetes and had at least 2 types of diabetes-related autoantibodies and abnormal sugar tolerance. Participants were randomly assigned to either the treatment group, which received a 14-day course of teplizumab, or the control group, which received a placebo. All participants received glucose tolerance tests regularly until the study was completed, or until they developed clinical type 1 diabetes – whichever came first.

During the trial, 72 percent of people in the control group developed clinical diabetes, compared to only 43 percent of the teplizumab group. The median time for people in the control group to develop clinical diabetes was just over 24 months, while those who developed clinical diabetes in the treatment group had a median time of 48 months before progressing to diagnosis.

The effects of the drug were greatest in the first year after it was given, when 41 percent of participants developed clinical diabetes, mainly in the placebo group. Many factors, including age, could have contributed to the ability of teplizumab to delay clinical disease, since at-risk children and adolescents are known to progress to type 1 diabetes faster than adults. Faster progression of type 1 diabetes is associated with a highly active immune system, which may explain the impact of immune system-modulating drugs like teplizumab.

NIH Funds Clinical Trials Using Genomics to Treat Chronic Diseases

NIH will fund clinical trials to assess the benefits, applicability, and efficacy of applying genomic medicine interventions to improve management of diseases such as high blood pressure, depression, and chronic pain.[30] The trials are part of the second phase of the Implementing Genomics in Practice (IGNITE) Network.[31] The trials are scheduled to begin in 2020.
The first trial will examine whether early access to patients' genomic data can help with treatment of high blood pressure, hypertension, and chronic kidney disease. Both hypertension and high blood pressure exacerbate end-stage kidney diseases, and all three conditions are more common among people of African ancestry than European and Asian descent. Researchers will compare whether medical intervention provided to those tested for a specific gene variant immediately after recruitment versus those tested three months later will have subsequent benefits.

[29] www.nih.gov/news-events/news-releases/drug-delays-type-1-diabetes-people-high-risk
[30] www.nih.gov/news-events/news-releases/nih-funds-clinical-trials-using-genomics-treat-chronic-diseases
[31] www.genome.gov/Funded-Programs-Projects/Implementing-Genomics-in-Practice-IGNITE-2-Pragmatic-Clinical-Trials-Network

The second trial will focus on pain and depression – two conditions where finding safe and effective drug treatments has been difficult. Because there are few clinically useful predictors for whether a depression treatment will be successful, patients often struggle to find effective therapies. To combat these issues, the study seeks to test whether patients with acute post-surgical pain, chronic pain, and depression have better clinical outcomes if pharmacogenomics guide opioid and antidepressant prescriptions.

These projects build upon the first phase of research from the IGNITE Network, which the National Human Genome Research Institute (NHGRI) funded in spring 2013 and focused on challenges and possible solutions to incorporating genomic information into electronic health records.

Study Helps Solve Mystery of How Sleep Protects Against Heart Disease

Researchers say they are closer to solving the mystery of how a good night's sleep protects against heart disease. In studies using mice, they discovered a previously unknown mechanism between the brain, bone marrow, and blood vessels that appears to protect against the development of atherosclerosis or hardening of the arteries — but only when sleep is healthy and sound.[32]

The discovery of this pathway underscores the importance of getting enough, quality sleep to maintain cardiovascular health and could provide new targets for fighting heart disease, the leading cause of death among women and men in the United States, the researchers said.

To learn more about the impact of sleep deficiency on cardiovascular disease, the researchers focused on a group of mice that were genetically engineered to develop atherosclerosis. They disrupted the sleep patterns of half the mice and allowed the other half to sleep normally. Over time, the mice with disrupted sleep developed progressively larger arterial lesions compared to the other mice. Specifically, the sleep-disrupted mice developed arterial plaques, or fatty deposits, that were up to one-third larger than the mice with normal sleep patterns. The sleep-disrupted mice also produced twice the level of certain inflammatory cells in their circulatory system than the control mice — and lower amounts of hypocretin, a hormone made by the brain that is thought to play a key role in regulating sleep and wake states.

The researchers also showed that sleep-deficient, atherosclerotic mice that received hypocretin supplementation tended to produce fewer inflammatory cells and develop smaller atherosclerotic lesions when compared to mice that did not get the supplementation. These results, they said, demonstrate that hypocretin loss during disrupted sleep contributes to inflammation and atherosclerosis. But they cautioned that more studies are needed, particularly in humans, to validate these findings and especially before experimenting with hypocretin therapeutically.

[32] McAlpine, S. et al. *Nature.* 2019 Feb; 566(7744): 383–387. doi: 10.1038/s41586-019-0948-2 PMCID: PMC6442744

Still, health experts say, targeting the newly discovered biological mechanism — a so-called neuro-immune axis — could be a breakthrough that one day leads to new treatments for heart disease, sleep, and other disorders.

FUNDING HISTORY

Fiscal Year	Amount[1, 2]
2017 [3]	$34,229,139,000
2018	$37,311,349,000
2019	$39,313,000,000
2020	$41,636,575,000
2021 Budget Request [4]	$38,693,631,000

[1] Appropriated amounts include discretionary budget authority received from both Labor/HHS appropriations that fund ICs as well as the Interior, Environment & Related Agencies appropriation that supports NIH Superfund Research activities. Also includes mandatory budget authority derived from the Special Type 1 Diabetes account. Includes NIGMS Program Evaluation financing of $824,443,000 in FY 2017, $922,871,000 in FY 2018, $1,146,821,000 in FY 2019, and $1,230,820,000 in FY 2020, and $741,000,000 in FY 2021. Includes CURES amounts of $352,000,000 in FY 2017, $496,000,000 in FY 2018, $711,000,000 in FY 2019, $492,000,000 in FY 2020, and $404,000,000 in the FY 2021 request.

[2] Excludes Ebola-related, Zika-related, and other supplemental appropriations and permissive and directive transfers.

[3] Reflects sequestration of the mandatory funding for Special Type 1 Diabetes Research account.

[4] Includes the consolidation of the Agency for Healthcare Research and Quality (AHRQ) activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ) in the amount of $355,112,000, including $98,452,000 for the Patient-Centered Outcomes Research Trust Fund. Figures prior to FY 2021 do not include amounts for the Agency for Healthcare Research and Quality (AHRQ). For information on AHRQ funding history, see the NIRSQ chapter of the NIH Congressional Justification.

SUMMARY OF REQUEST NARRATIVE

The FY 2021 President's Budget request provides a program level of $38.7 billion for NIH, which is $3.0 billion less than the FY 2020 Enacted level of $41.7 billion.

The following summary references program level funding, which is the sum of discretionary budget authority in the Department of Labor, Health and Human Services, and Education, and Related Agencies appropriations ($37.6 billion in FY 2021); discretionary budget authority in the Department of the Interior, Environment, and Related Agencies appropriations dedicated to the Superfund Research program ($73.7 million in FY 2021); mandatory budget authority provided for Type 1 Diabetes research ($150.0 million in FY 2021); and Program Evaluation Financing for the National Institute of General Medical Sciences under Section 241 of the Public Health Service Act ($741.0 million in FY 2021).

The request includes the consolidation into NIH of Agency for Healthcare Research and Quality (AHRQ) activities as a new National Institute for Research on Safety and Quality (NIRSQ). The NIH FY 2021 discretionary budget authority request includes $256.7 million for NIRSQ and the NIH FY 2021 program level includes an additional $98.5 million for the related Patient-Centered Outcomes Research Trust Fund (PCORTF).

The primary budget mechanisms discussed below include allocations by mechanism of Program Evaluation Financing and Type 1 Diabetes funds. In addition, the mechanism detail for FY 2021 reflects the allocation of discretionary budget authority for NIRSQ. The Superfund Research program and PCORTF are as lump-sum amounts within the NIH mechanism tables.

In FY 2021, NIH will continue providing upfront funding for certain projects, as appropriate, to facilitate efficient management of resources across multiple years. In general, NIH discretionary research project grants are awarded for more than one year and funded incrementally; each year's commitment is obligated from that year's appropriation. Grants are classified as Competing in the first year of award or renewal, and Non-competing in the remaining years of each award. Certain categories of NIH grants are awarded for multiple years with the full funding provided up front. This includes the NIH Director's New Innovator Award (DP2) and the NIH Research Enhancement Award (R15). The latter consists of two programs, the Academic Research Enhancement Award (AREA) for Undergraduate-Focused Institutions, and the Research Enhancement Award Program (REAP) for Health Professional Schools and Graduate Schools. In addition, full funding can be provided up front for other NIH grants and cooperative agreements as appropriate in special circumstances. Situations that may benefit from such an approach can include, but are not limited to, appropriations for new programs, rapid increases in funding, or variable outyear funding streams (e.g., under the 21st Century Cures Act). The use of upfront funding for new programs makes some base funding available for competing awards in the following year. Up-front funding has increased over the last few years (from two percent of total research grant dollars to nearly six percent in FY 2019), due in part to the large Congressional increases for Alzheimer's disease research. FY 2019 also included a one-time increase in up-front funding due to the HEAL Initiative, because it changed from two-year to one-year money; as a result, more than a year's worth of HEAL appropriations were obligated in FY 2019.

Research Project Grants (RPGs)
The FY 2021 President's Budget provides $22.1 billion for RPGs, which is $1.8 billion less than the FY 2020 level. This amount would fund 9,505 Competing RPGs, or 1,874 less than for the FY 2020 level. It would also support 30,109 Noncompeting RPGs, 601 more than the FY 2020 level. In addition, the projected average cost for Competing RPGs of approximately $541,000 would be 1.1% below the FY 2020 projected average cost of nearly $547,000.

- **Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) RPGs.** The FY 2021 President's Budget provides $1,035.6 million for SBIR/STTR program grants, which is $83.3 million below the FY 2020 level. The statutory minimum set-aside requirement of 3.65% for NIH-wide SBIR/STTR support is achieved in FY 2021.

Research Centers
The FY 2021 President's Budget provides $2,405.8 million for Research Centers, which is $258.0 million less than the FY 2020 level. This amount would fund 1,135 grants, 102 less than the FY 2020 level.

Other Research
The FY 2021 President's Budget provides $2,440.5 million for this mechanism, which is $223.0 million less than the FY 2020 level. This amount would fund 7,014 grants, which is 494 less than the number of awards projected for FY 2020.

Training
The FY 2021 President's Budget provides $847.7 million for research training, which is $62.2 million below the FY 2020 level. This amount would fund 16,305 Full-Time Trainee Positions (FTTPs), which is 1,342 fewer than planned for FY 2020.

Research & Development (R&D) Contracts
The FY 2021 President's Budget provides $3,077.1 million for R&D contracts, which is $272.3 million less than the FY 2020 level. The requested amount would fund an estimated 2,409 contracts, or 254 fewer than the FY 2020 level.

- **SBIR/STTR R&D Contracts.** The FY 2021 President's Budget includes a $74.4 million set-aside within the R&D Contracts mechanism for support of qualified SBIR/STTR contracts.

Intramural Research (IR)
The FY 2021 President's Budget provides $4,076.6 million for IR, which is $369.3 million less than the FY 2020 level.

Research Management and Support (RMS)
The FY 2021 President's Budget provides $1,926.1 million for RMS, which is $88.5 million less the FY 2020 level.

Office of the Director (OD)
The FY 2021 President's Budget provides $2,208.1 million for OD, which is $196.3 million less than the FY 2020 level.

- **Common Fund (CF)**
  Funding of $596.5 million is allocated for CF-supported programs. This amount is $42.6 million below the FY 2020 level.

- **Office of Research Infrastructure Programs (ORIP)**
  Funding of $268.6 million is allocated for ORIP. This amount is $19.6 million below the FY 2020 level.

- **Other**
  The $1,343.0 million allocated for OD components other than the Common Fund or the Office of Research Infrastructure Programs is a net decrease of $134.1 million from the FY 2020 level. This is due, in part, to a decrease in the portion of funding authorized by the 21st Century Cures Act that is managed by OD, from $157.0 million to $109.0 million. The 21st Century Cures Act resources for FY 2021 in OD consists of $109.0 million for the *All of Us* Research Program. The request does not include funding for Regenerative Medicine, for which the final year of 21st Century Cures Act funding was FY 2020.

Buildings & Facilities (B&F)
The FY 2021 President's Budget provides $315.0 million for infrastructure sustainment projects associated with the B&F program, which is $85.0 million more than the FY 2020 level. This amount includes $300.0 million for NIH's Buildings and Facilities appropriation, an increase of $100.0 million from the FY 2020 level, and $15.0 million within the appropriation for the National Cancer Institute (NCI) for facility repair and improvement activities at NCI's Frederick, Maryland, facility. The FY 2021 amount of $15.0 million is an estimate and may increase up to the $30.0 million allowable by law as needs are evaluated.

Superfund Research Program
The FY 2021 President's Budget provides $73.7 million, which is $7.3 million less than the FY 2020 level.

Program Evaluation Financing
The FY 2021 President's Budget provides $741.0 million for Program Evaluation Financing purposes in NIGMS, which is $489.8 million less than the FY 2020 level.

OUTPUTS AND OUTCOMES

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
SRO-1.5 By 2020, increase our understanding of cancer trends and outcomes in the context of disparities and population subgroups through expansion of coverage and representation of the US population in the Surveillance, Epidemiology and End Results (SEER) Program registries. (Outcome)	FY 2019: The SEER Program has successfully created linkages with Genomic Health, Inc. (GHI) for the collection of genomic data and with pharmacy vendors for the collection of pharmacy data. Target: Expand SEER to include links with 1-2 outside sources such as biospecimen acquisition, genomics and molecular profile data. (Target Met)	Provide trends and rates specific to the clinically relevant cancer subtypes represented by molecular characterization of each tumor.	N/A	N/A
SRO-1.6 By 2020, determine the effectiveness of an evidence-based, patient-centered multicomponent fall injury prevention strategy in adults 75 years of age and older. (Outcome)	FY 2019: The follow-up of all the participants enrolled in this clinical trial has been completed. Target: Complete follow-up of participants enrolled in the trial testing the effectiveness of the evidence-based, patient-centered multicomponent fall injury prevention strategy and analyze trial data. (Target Met)	Complete analyses of secondary outcome data. These outcomes include patient concerns about falling, all falls, all fall-related injuries, physical function, disability, anxiety and depression.	N/A	N/A
SRO-2.1 By 2023, develop, optimize, and evaluate the effectiveness of nano-enabled immunotherapy (nano-immunotherapy) for one cancer type. (Output)	FY 2019: Two unique nanodelivery systems for effective anti-cancer immunotherapeutics were further optimized in different animal models and showed promising results for consideration in clinical trials. Target: Further optimize top two candidate	Further optimize the top candidate nanoformulation for co-delivery of antigens, adjuvants and immuno-modulators and evaluate its efficacy and long-lasting immunity (over 3 months) in preclinical models	Further optimize the top candidate nanoformulation for co-delivery of antigens, adjuvants and immuno-modulators and evaluate its efficacy towards near and distance metastatic lesions in preclinical	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	nanoformulations for co-delivery of multiple antigens to enhance anti-tumor response in one animal model. (Target Met)	with established tumors.	models with established tumors.	
SRO-2.3 By 2019, evaluate the impact of a community-level combination prevention package (which includes universal HIV testing and intensified provision of HIV antiretroviral therapy and care) on population-level HIV incidence in the developing world. (Outcome)	FY 2019: Researchers completed data analyses for evaluating the impact of a community-level combination prevention package on population-level HIV incidence. Target: Complete data analyses to evaluate the impact of a community-level combination prevention package on population-level HIV incidence. (Target Met)	N/A	N/A	N/A
SRO-2.4 By 2025, increase the number of potential treatment options for communication disorders that are being tested in clinical trials by adding one new treatment option per year. (Outcome)	FY 2019: An NIH-funded study has initiated testing one new potential treatment option for congenital cytomegalovrius (CMV)-induced hearing loss that develops in the first year of life. This study is enrolling infants born infected with CMV yet who have no clinical symptoms (asymptomatic) to treat them with antiviral drugs. Target: Initiate testing one new potential treatment option for a hearing disorder. (Target Met)	Initiate testing one new potential treatment option for a taste disorder.	Initiate testing one new potential treatment option for a disorder affecting voice, speech, or language.	N/A
SRO-2.5 By 2021, develop three non-	FY 2019: All five teams in the Audacious Goals	Translate two novel imaging technologies	Complete development of three	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
invasive imaging technologies that can image retinal cell function and circuitry. (Output)	Functional Imaging Consortium have integrated measurements of cell function with anatomical imaging. Target: Integrate measurements of cell function with anatomical imaging. (Target Met)	from animal studies into human participants.	non-invasive imaging technologies which image retinal cell function and circuitry.	
SRO-2.6 By 2020, investigate the pathways and mechanisms of how seven environmental agents can alter epigenetic processes such as DNA methylation, recruitment of specific histone modifications, and chromatin remodeling to better determine if these changes can be inherited. (Output)	FY 2019: Researchers identified sex differences in three environmentally induced epigenomic signatures in three different mouse tissues. Target: Determine and identify, if present, sex differences in three environmentally induced epigenomic signatures in three different mouse tissues. (Target Met)	Determine and identify, if present, sex differences in four additional environmentally induced epigenomic signatures in three different mouse tissues.	N/A	N/A
SRO-2.7 By 2022, file Phase II Investigational New Drug (IND) application with the FDA for a therapy to treat geographic atrophy in age-related macular degeneration (AMD) using patient-derived stem cells. (Outcome)	FY 2019: The IND application was submitted in 2019, but FDA has not yet given approval to enroll patients into Phase I clinical trial. Target: Recruit three AMD patients into Phase I clinical trial. (Target Not Met but Improved)	Recruit 3 AMD patients into Phase I clinical trial.	Complete Phase I trial enrollment to treat a total of 12 AMD patients.	N/A
SRO-2.8 By 2023, advance the development of three novel drug or biologic therapeutic candidates	FY 2019: For the target mechanisms of inflammation and synaptic plasticity, 12 candidate therapeutic agents were	Complete preclinical proof of concept in animal models of AD for 3-5 new	Initiate Investigational New Drug-enabling studies for 2-3 new	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
for Alzheimer's disease (AD) or related dementias toward the point of entry into Phase I human studies. (Output)	selected to undergo preclinical optimization studies. Target: For each of the novel therapeutic targets, select 3-5 candidate therapeutic agents for entry into preclinical optimization studies. (Target Exceeded)	candidate therapeutics.	candidate therapeutics.	
SRO-2.9 By 2022, evaluate the safety and effectiveness of 1-3 long-acting strategies for the prevention of HIV. (Outcome)	FY 2019: NIH-funded investigators completed final analysis of an open-label extension study that built on the findings of an earlier trial and aimed to assess the continued safety of the dapivirine vaginal ring and study participants' adherence to its use. Target: Strategy 3: Complete final analysis of an open-label extension study that builds on the findings of an earlier trial and aims to assess the continued safety of the dapivirine vaginal ring in a more real-world context and study participants' adherence. (Target Met)	Strategy 1: Complete follow-up of participants in at least one of the studies testing the safety, tolerability, and effectiveness of VRC01.	Strategy 1: Analyze data of two studies testing the safety, tolerability, and effectiveness of VRC01 broadly neutralizing antibody (bnAb).	N/A
SRO-2.10 By 2024, develop methods for the regeneration of functional tissues of the human dental, oral, and craniofacial complex to enable initiation of human Phase I clinical trials. (Outcome)	FY 2019: Seven interdisciplinary translational projects have advanced in the FDA review process. Target: Submit an Investigational New Drug (IND) application for an FDA-approved tissue regeneration combination	Initiate pre-clinical animal studies that will lead to the development of regenerative medicine therapies of human dental, oral, and craniofacial diseases and conditions.	The Resource Centers will facilitate the development of five Investigational New Drug (IND)/Investigational Device Exemption (IDE) applications from the current pool of Interdisciplinary	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	product. (Target Met)		Translational Projects.	
SRO-2.12 By 2021, develop, validate, and/or disseminate 3-5 new research tools or technologies that enable better understanding of brain function at the cellular and/or circuit level. (Output)	FY 2019: The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative Public-Private Partnership Program initiated testing of brain stimulation devices for six new therapeutic indications in humans and continued to enable current and potential BRAIN investigators to gain access to medical device tools and technologies from some of the top medical device manufacturers. Target: Test new and/or existing brain stimulation devices for two new therapeutic indications in humans through the BRAIN Public Private Partnership. (Target Exceeded)	Provide broad access to new research approaches and techniques for acquiring fundamental insight about how the nervous system functions in health and disease.	Expand our understanding of brain function at the cellular or circuit level using 3-5 new tools and technologies.	N/A
SRO-2.13 By 2023, advance the development of 1-2 new drugs and/or other therapeutic candidates for neurological diseases from lead optimization or device development toward the point of preparedness for first-in-human studies. (Output)	FY 2019: A total of seven therapeutic and device candidates have been identified and advanced for animal toxicology studies. Target: Identify and characterize 2-4 therapeutic or device candidates in preparation for animal toxicology studies. (Target Exceeded)	Initiate animal toxicology studies for 1-2 therapeutic or device candidates.	Determine the margin of safety for 1-2 therapeutic or device candidates.	N/A
SRO-3.1 By 2025, identify neurobehavioral precursors or consequences of adolescent substance use	FY 2019: Research in animal models has demonstrated that adolescent alcohol exposure results in a persistent loss of	Examine how individual differences in neurobiology contribute to	Conduct preclinical studies to identify persistent neurobiological adaptations that	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
or other childhood experiences. (Outcome)	cholinergic cells in the basal forebrain, an adaptation associated with cognitive dysfunction. Target: Continue to evaluate the impact of adolescent alcohol or other substance use on brain development. (Target Met)	adolescent substance taking behavior and related health outcomes.	occur as a result of exposure to alcohol during adolescence.	
SRO-3.2 By 2023, establish the feasibility of using one emerging technology to safely and non-invasively obtain real time data on human placenta development and function during pregnancy. (Outcome)	FY 2019: NIH developed the Placental Atlas Tool to provide a collaborative research and discovery platform for the placental research community. Target: Develop specifications for a curated dataset to serve as a resource for placental research, including identifying research gaps and discovering potential biomarkers and therapeutic targets for drug delivery. (Target Met)	Identify two biomarkers that are associated with placental development and/or function.	Utilize one innovative technology to characterize longitudinal changes in normal vs. abnormal placenta during pregnancy.	N/A
SRO-3.9 By 2020, identify two molecular-targeted therapies for disorders of the immune system that affect children. (Outcome)	FY 2019: Researchers have treated four patients with treatment-resistant juvenile dermatomyositis (JDM) with a Janus Kinase (JAK) inhibitor for over one year. Patients have shown clinical and laboratory evidence of a beneficial and sustained response. Target: Continue an interventional clinical study of a molecularly targeted therapy for a disorder of the immune system that affects children.	Complete an interventional clinical study of a molecularly targeted therapy for a disorder of the immune system that affects children.	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	(Target Met)			
SRO-4.1 By 2020, enable 1-3 Bridging Interventional Development Gaps (BrIDGs) projects to have sufficient pre-clinical data for therapeutic agents in order to apply for Investigational New Drug (IND) approval from the FDA. (Output)	FY 2019: The BrIDGs program completed necessary studies for a project to file an IND application with FDA. Target: Initiate formal GLP toxicology studies for 1-3 projects. (Target Met)	Enable 1-3 BrIDGs projects to have sufficient pre-clinical data for therapeutic agents in order to apply for IND approval from the FDA.	N/A	N/A
SRO-4.3 By 2020, advance our characterization and understanding of the cellular and genetic components that make up the diverse composition of most tumors. (Outcome)	FY 2019: Researchers have identified cells and associated molecules in numerous cancer types that show promise in understanding and managing cancer. Examples include specific immune cells in breast cancer, neuroblastoma, head and neck, and pancreatic cancer Target: Identify the role various cellular components play in the phenotype of the 3 cancers. (Target Met)	Based on new understanding of tumor composition, develop three computational models to explore new knowledge and treatments.	N/A	N/A
SRO-4.4 By 2019, discover the molecular basis for 60 rare diseases. (Output)	FY 2019: The molecular bases of 28 rare diseases were discovered. Target: Discover the molecular bases of an additional 10 rare diseases (Target Exceeded)	N/A	N/A	N/A
SRO-4.8 By 2019, establish a sharable collection of positive Zika virus (ZIKV) biospecimens to increase	FY 2019: A sharable biorepository, containing biospecimens from ZIKV-infected blood donors who participated in the 2016-	N/A	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
knowledge of viral infection and associated host immune response to help evaluate potential strategies to ensure the safety of the blood supply. (Output)	2018 US Natural History Study, was successfully established and completed. Target: Complete the establishment of a shareable repository of Zika biospecimens, analyze data from a US Zika database, establish utility of blood screening for Zika virus, and assess Zika transfusion-transmission risks in animal models. (Target Met)			
SRO-4.9 By 2020, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD). (Output)	FY 2019: A pre-clinical study of a novel opiate withdrawal therapy was conducted, and a clinical trial of a therapy for both opioid withdrawal and associated insomnia was also conducted. Target: Conduct one pre-clinical study and one clinical trial to develop non-opioid based medications to treat OUD that may avoid the risks of opioid dependence and overdose. (Target Met)	Conduct one pre-clinical and one clinical study of a longer acting formulation of a medication for the treatment of opioid use disorders or opioid overdose.	N/A	N/A
SRO-4.10 By 2020, design and develop novel dental composite resins that demonstrate superiority over the currently used restorative materials. (Output)	FY 2019: Discussions with the FDA facilitated articulation and achievement of milestones for commercial viability. Target: Implement regulatory feedback received by the FDA to demonstrate safety and effectiveness.	One patent application of a novel resin will be completed, reflecting the priorities identified by the FDA.	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	(Target Met)			
SRO-4.11 By 2020, create a model system that recreates key features of human type 1 diabetes (T1D) autoimmunity for use in therapeutics development and testing. (Outcome)	FY 2019: A system was developed for rapid and high-fidelity insertion of two T1D-associated risk alleles into a human induced pluripotent stem cell (iPSC) line. Target: Develop a system for rapid and high-fidelity insertion of two T1D-associated risk alleles into a human induced pluripotent stem cell (iPSC) line. (Target Met)	Use in vivo model(s) carrying iPSC-derived human beta cells to test the efficacy of two approaches aimed at enhancing beta cell viability and/or expansion.	N/A	N/A
SRO-4.12 By 2019, evaluate weight-related, psychosocial, and metabolic outcomes in response to treatment of adolescents with severe obesity. (Outcome)	FY 2019: The impact of the impact of bariatric surgery for severe obesity during adolescence on weight-related and psychosocial and behavioral outcomes was evaluated. Target: By 2019, evaluate the impact of bariatric surgery for severe obesity during adolescence on weight-related and psychosocial and behavioral outcomes. (Target Met)	N/A	N/A	N/A
SRO-4.14 By 2020, identify a total of three effective strategies to reduce modifiable health risk factors associated with premature mortality in people with serious mental illness (SMI). (Outcome)	FY 2019: Researchers tested three health risk reduction models with the potential to reduce premature mortality in adults with SMI. Target: Conduct testing of three health risk reduction models that have potential to reduce premature mortality in adults with	Conduct testing of an additional three health risk reduction models that have potential to reduce premature mortality in adults with SMI.	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	SMI. (Target Met)			
SRO-4.15 By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations. (Output)	FY 2019: Researchers tested the *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide's* two-question screening tool to determine its predictive ability in identifying future risk for alcohol-related problems in an underage population. Target: Test a screening and brief alcohol intervention in an underage population. (Target Met)	Test a behavioral therapy for intervening with alcohol misuse in an underage population.	Test another behavioral therapy for intervening with alcohol misuse in an underage population.	N/A
SRO-5.1 By 2020, develop and test the effectiveness of two strategies for translating cancer knowledge, clinical interventions, or behavioral interventions to underserved communities in community-based clinical settings. (Outcome)	FY 2019: Two U54 Partnerships to Advance Cancer Health Equity finalized testing and validating evidence-based interventions and tools to help translate basic cancer knowledge and clinical or behavioral interventions to underserved communities across the United States. They continue to work with various community-based organizations to disseminate these interventions and tools. Target: Finalize testing and validating the strategies to translate basic cancer knowledge, clinical or behavioral interventions to underserved communities and into clinical practice. (Target Met)	Finalize testing and validating the strategies to translate basic cancer knowledge, clinical or behavioral interventions to underserved communities and into clinical practice.	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
SRO-5.2 By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders (SUD). (Outcome)	Note: SRO-5.2 will begin reporting in December 2020.	Conduct 3-5 pilot studies to test the efficacy of promising prevention interventions for SUD.	Complete 1-2 pilot studies to test the efficacy of a prevention intervention for SUD.	N/A
SRO-5.3 By 2023, identify risk and protective alleles that lead to one novel therapeutic approach, drug target, or pathway to prevention for late-onset Alzheimer's disease. (Output)	FY 2019: The Alzheimer's Disease Sequencing Project (ADSP) Follow-Up Phase has begun its analysis of genomic regions of interest using whole genome sequence data from ethnically diverse cohorts. The ADSP has continued its confirmation of genomic regions identified in the Discovery Phase of the Project. Genetic data for all phases of the ADSP have been harmonized. Target: Begin analysis of genomic regions of interest in the ADSP Discovery Follow-Up Phase using whole genome sequence data from ethnically diverse cohorts. Continue confirmation of genomic regions of interest in the Discovery Phase using samples from the Follow-Up Phase. Continue harmonization of Discovery Phase and Follow-Up Phase datasets. (Target Met)	Continue analysis of ADSP Discovery Follow-Up Phase in ethnically diverse cohorts. Continue confirmation of genomic regions of interest from Discovery Phase and Discovery Follow-Up Phase in ethnically diverse datasets. Compare data on genomic regions of interest by ethnicity.	Continue analysis of ADSP Discovery Follow-Up Study in ethnically diverse cohorts. Continue confirmation of genomic regions of interest from Discovery Phase and Discovery Follow-Up Phase in ethnically diverse datasets. Begin harmonization of phenotypic data with ADSP genetic data across multiple types of study approaches from large epidemiology and clinical cohorts that are outside of the ADSP.	N/A
SRO-5.8 By 2022, obtain pre-clinical and clinical data from newly initiated and current studies to evaluate 1-2 HIV vaccine candidate(s). (Outcome)	FY 2019: Evaluated two alternative HIV vaccine candidates' suitability for human testing. Target: Evaluate 1-2 alternative HIV vaccine	Further explore identification of correlates of protection in non-human primate animal models.	Enroll half (1,900) of the 3,800 participants needed for a Phase 3 vaccine study.	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	candidates' suitability for human testing. (Target Met)			
SRO-5.10 By 2020, assess the effectiveness of five to seven interventions that focus on eliminating health disparities by utilizing community partnerships to conduct intervention research that will foster sustainable efforts at the community level that will impact disparate conditions. (Output)	FY 2019: The intervention projects have completed approximately 90 percent of enrollment. Projects have initiated assessments of the interventions' outcomes and are developing plans for data sharing and dissemination of results. Target: Assess intervention progress and collect fourth year assessment variables. (Target Met)	Complete analyses of five to seven community-based participatory research interventions to determine effectiveness in impacting health disparity conditions.	N/A	N/A
SRO-5.12 By 2020, develop and/or characterize 3 mouse models for investigation of properties and functions of skin stem cells that can be used to advance research on wound healing, tissue engineering, or skin cancer. (Outcome)	FY 2019: Researchers characterized mouse models in which stem cell participation in wound healing is impaired or could be enhanced. One study showed that a population of fat precursor cells needed to repair skin wounds is decreased in aged mice. Two other studies in mice uncovered different mechanisms by which wound healing by stem cells in the skin might be improved. Target: Develop and/or characterize a mouse model in which skin stem cell participation in wound repair is impaired. (Target Met)	Describe the role of stem cells in skin cancer development by creating traceable stem cells that allow researchers to study cancer development from its earliest events.	N/A	N/A
SRO-5.13 By 2022, complete research to the pre-clinical stage of	FY 2019: Researchers developed methods to non-invasively deliver	Initiate research of a prototype technology that uses acoustic,	Conduct research on continued development and	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
development of a new or significantly improved targeted, minimally invasive biomodulation technology for therapy. (Outcome)	therapeutics across the blood-brain barrier and track the exact dose and location the drugs reach to treat brain disease. Target: Initiate research to test and refine one new or improved technology that uses acoustic, optical or electromagnetic waves to manipulate cells for treatment of illness. (Target Met)	optical, or electromagnetic waves as a test case in a specific disease.	preliminary testing of one prototype technology that uses acoustic, optical, or electromagnetic waves to manipulate cells for treatment of a specific disease and begin to develop a plan for initiating the regulatory process.	
SRO-5.14 By 2020, evaluate the effectiveness of one intervention to reduce death and/or neurodisability in pre-term or in full term infants with life-threatening conditions. (Outcome)	FY 2019: The Transfusion of Prematures (TOP) Trial completed enrollment of 1,824 participants. Target: Complete enrollment in transfusion study. (Target Met)	Complete follow-up on subjects enrolled in a comparative-effectiveness study on two surgical procedures to treat intestinal perforation due to necrotizing enterocolitis in infants.	N/A	N/A
SRO-5.15 By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations. (Outcome)	FY 2019: Researchers demonstrated the efficacy of interventions involving brief motivational interviewing and a supplemental activity for reducing alcohol misuse among college age individuals. Target: Develop an intervention to prevent or reduce alcohol misuse among college age individuals. (Target Met)	Develop a digital technology-based intervention to prevent or reduce alcohol misuse in underage individuals.	Disseminate information to the public about evidence-based interventions for underage populations.	N/A
SRO-5.16 By 2021, conduct research to support pharmaceutical labeling changes for five drugs, to reflect safe and	FY 2019: The multi-center digoxin study, which aims to study pharmacokinetics and safety of digoxin in children less than six	Obtain preliminary pharmacokinetic results to help assess the safety for mothers and infants	Assess pharmacokinetics, pharmacodynamics, and safety of 5 drugs	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
appropriate dosing and use specifically in children. (Outcome)	months old, launched in August 2019. The study is currently enrolling participants. Target: Begin one Phase III clinical trial for drug development. (Target Met)	of at least three common, off-patent drugs when used by breastfeeding women.	in pediatric populations.	
SRO-5.17 By 2022, develop and test the effectiveness of three strategies to enhance end-of-life and palliative care. (Outcome)	FY 2019: Studies found that a family-centered advance planning intervention improved end-of-life care communication between individuals living with HIV and their family surrogate decision-makers. Target: Test at least one novel strategy for improving care for patients with advanced illness through shared decision-making. (Target Met)	Develop and test one novel strategy for improving end-of-life/palliative care through better support of family members and informal caregivers.	Develop and test at least one effective intervention for improving quality of life for patients at the end of life through enhanced shared decision-making and support of informal caregivers.	N/A
SRO-6.1 By 2023, perform comparative effectiveness studies to test five therapies for prevention or treatment of type 2 diabetes. (Outcome)	FY 2019: The baseline data from the three Restoring Insulin Secretion protocols (pediatric medication, adult medication, and adult surgery) were analyzed. Target: Analyze the baseline data from the three Restoring Insulin Secretion protocols to understand differences between adult and pediatric individuals with pre-diabetes or newly diagnosed type 2 diabetes. (Target Met)	Complete final visits and analyze the data from the Restoring Insulin Secretion adult medication study.	Complete all final participant visits in the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study, according to the study protocol.	N/A
SRO-6.2 By 2025, advance 1-2 new or repurposed compounds	FY 2019: Researchers conducted a human laboratory study to evaluate	Evaluate one compound with potential for treating	Conduct a preclinical evaluation of a novel or repurposed	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
that act on neurobiological targets that may have the potential for treating alcohol or other substance use disorders. (Outcome)	the safety of the ghrelin receptor blocker PF-5190457 as a potential treatment for alcohol use disorder when administered in combination with alcohol. Target: Conduct at least one human laboratory study to evaluate the safety and efficacy of candidate compounds for treating alcohol or other substance use disorders. (Target Met)	alcohol and other substance use disorders in a clinical trial.	compound that acts on neurobiological targets implicated in alcohol use disorder.	
SRO-7.3 By 2020, develop and/or evaluate two treatment interventions using health information technology (HIT) to improve patient identification, treatment delivery or adherence for substance use disorders and related health consequences. (Output)	FY 2019: Development of five promising interventions to prevent or treat substance use disorders or to improve medication adherence have been initiated. Target: Develop and/or evaluate two HIT-based interventions to prevent or treat substance use disorders or to improve medication adherence. (Target Exceeded)	Develop and test 1-2 FDA-approved digital therapeutic interventions for substance use disorder treatment and/or medication adherence.	N/A	N/A
CBRR-1.1 Provide research training for predoctoral trainees and fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2019: Award rate to comparison group reached 11 percent. Target: N ≥ 10% (Target Met)	N ≥ 10%	N ≥ 10%	N/A
CBRR-1.2 Provide research training for postdoctoral fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2019: Award rate to comparison group reached 15 percent and exceeded target by five percent. Target: N ≥ 10%	N ≥ 10%	N ≥ 10%	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	(Target Exceeded)			
CBRR-2 Promote data sharing and provide information in real time through the NIH Business System (NBS) by developing, integrating, deploying and maintaining business modules. (Output)	FY 2019: NBS implemented Fund Configuration Initiative as planned. Target: (Development [Dev]) Continue development of remediation activities to comply with HHS Accounting Treatment Manual and other Treasury Mandates to increase accuracy and functionality of the NBS. (Target Met)	(Deployment [Dep]) Conduct priority deployment activities for the Funds Configuration Initiative to comply with one of the NIH Corrective Action Plan remediation efforts.	(Development [Dev]) Continue to conduct priority deployment activities for the NIH Corrective Action Plan remediation efforts.	N/A
CBRR-4 By 2021, produce and phenotype 2,500 knockout mouse strains to enhance the capacity of researchers to investigate the in vivo function of mammalian genes and identify new models of human disease. (Outcome)	FY 2019: Over 600 knockout juvenile lines were characterized (phenotyped). Target: Deliver phenotyping on 600 knockout juvenile lines. (Target Exceeded)	Deliver phenotyping on 600 knockout juvenile lines.	Provide a cumulative total of 2,500 knockout mouse juvenile lines and associated resources to support research into gene function and human diseases.	N/A
CBRR-5 By 2019, enhance the Clinical and Translational Science Awards (CTSA) Program by establishing resources, processes and guidelines to streamline and accelerate the implementation of multisite clinical trials. (Output)	FY 2019: Nine active multi-site clinical trials are active in the Trial Innovation Network of the CTSA program. Target: Launch at least two multi-site clinical trials within the CTSA trial innovation network. (Target Met)	N/A	N/A	N/A
CBRR-6 By 2019, launch and establish a Biomedical Citizen Science Hub to serve as an online collaboration space for biomedical	FY 2019: There are more than 300 registered users of the site and more than five subgroups for the Biomedical Citizen Science Hub.	N/A	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
citizen science research efforts in cancer biology. (Output)	Target: Establish 200-300 registered users of the site and 5 subgroups for the Biomedical Citizen Science Hub. (Target Met)			
CBRR-9 By 2020, enroll a total of 3,010 participants in GenomeConnect, ClinGen's Patient Registry. (Output)	FY 2019: A cumulative 2,584 participants were enrolled in GenomeConnect. Target: Enroll 2,002 cumulative participants in GenomeConnect. (Target Exceeded)	Enroll a total of 3,010 participants in GenomeConnect, ClinGen's Patient Registry.	N/A	N/A
CBRR-10 By 2020, enroll 180 children into the Pediatric Heart Network (PHN) to support a research resource for investigators conducting research in congenital heart disease across the age spectrum. (Output)	FY 2019: More than 50 children were enrolled in the PHN in 2019. Target: Enroll 50 children with complex congenital heart disease in a clinical research study. (Target Met)	Enroll 50 children with complex congenital heart disease in a clinical research study.	N/A	N/A
CBRR-18 By 2021, develop and validate a new protocol for dementia assessment for use in large nationally representative samples. (Outcome)	FY 2019: Data collection is complete in US, Mexico, and England. Results from these efforts were reviewed and used to refine assessment protocols to increase sensitivity and specificity. Target: Review results from the assessment protocol as deployed in the US in 2016-2017 and in other countries in 2017 and 2018. Refine protocol as needed to increase sensitivity and specificity.	Make data from the Harmonized Cognitive Assessment Protocol (HCAP) publicly available to the research community and initiate a follow-up study to the HCAP.	Complete follow-up assessment in the Health and Retirement Study using the refined HCAP.	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	(Target Met)			
CBRR-19 By 2019, identify and characterize 1,900 immune epitopes from infectious pathogens and allergens for deposit into the Immune Epitope Database (www.iedb.org) to accelerate development of more effective vaccines and immune-based therapeutics. (Output)	FY 2019: 199 T cell and 275 B cell epitopes from infectious disease pathogens and 312 T cell epitopes from allergens were identified and characterized. Target: Identify and characterize 650 T cell and 250 B cell epitopes from infectious pathogens and 100 T cells epitopes from allergens to accelerate development of more effective vaccines and immune-based therapeutics. (Target Not Met)	N/A	N/A	N/A
CBRR-20 By 2020, advance the preclinical development of ten candidate products (e.g., vaccines, therapeutics) to combat infectious diseases. (Outcome)	FY 2019: More than 10 vaccine and therapeutic candidate products were advanced in FY 2019. Target: Advance the preclinical development of three vaccine and/or therapeutic candidate products. (Target Exceeded)	Advance the preclinical development of four vaccine and/or therapeutic candidate products.	N/A	N/A
CBRR-21 By 2020, establish and implement a national collaborative Pilot and Feasibility (P&F) program that utilizes specialized equipment, and expertise in nonmalignant hematology that are available through the Cooperative Centers of Excellence in Hematology (CCEH). (Output)	FY 2019: Eight P&F projects involving collaborations outside of the hematology Centers were supported in FY 2019. Target: Support two P&F projects involving collaboration outside the hematology Centers. (Target Met)	Support four P&F projects involving collaboration outside the hematology Centers.	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
CBRR-22 By 2020, establish a reference map that will serve as the framework to understand the development of the human urinary tract. (Outcome)	FY 2019: Five types of epithelial cells in the human prostate were identified and mapped. Target: Identify and map at least five specific cell types or subtypes within the kidney, urinary outflow tract, and/or prostate. (Target Met)	Generate and release the human/mouse comparative atlases to the general public.	N/A	N/A
CBRR-23 By 2019, provide access to laboratory and data analytical services and a data repository that will allow the NIH extramural research community the capability to add or expand the inclusion of environmental exposure analysis in children's health research. (Output)	FY 2019: NIH supported approximately 15,000 sample analyses involving 7 new studies. The results from 2,322 sample analyses or two studies are available to the broader scientific community; the results from an additional 14,741 sample analyses or 10 studies are currently under embargo pending initial client publication. Target: Support analysis for at least 10 additional studies (or about 10,000 sample analyses) and make the results from about 10 studies or 10,000 sample analyses available to the broader scientific community. (Target Met)	N/A	N/A	N/A
CBRR-24 By 2019, pilot test and assess alternative funding mechanisms such as program-focused awards. (Output)	FY 2019: The proportion of NIGMS grantees who are Maximizing Investigators' Research Award (MIRA) recipients increased by five percentage points from FY 2017 to FY 2018. Target: Expand by five percent the proportion of	N/A	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	NIGMS-supported investigators funded by active R01-equivalent awards who are MIRA recipients. (Target Met)			
CBRR-25 Increase the total number of mentored research career development experiences for trainees from diverse backgrounds, including groups underrepresented in biomedical research, to promote individual development and to prepare them for a range of research-related careers. (Output)	FY 2019: Trainees from diverse backgrounds received a total of 3,797 career experiences across all career stages. Target: 3,522 career experiences across all career stages. (Target Exceeded)	3,539 career experiences across all career stages	3,540 career experiences across all career stages	N/A
CBRR-26 Maintain the yearly number of undergraduate students with mentored research experiences through the IDeA (Institutional Development Award) Networks of Biomedical Research Excellence (INBRE) program in order to sustain a pipeline of undergraduate students who will pursue health research careers. (Output)	FY 2019: Approximately 1,450 undergraduate students participated in mentored research experiences, consistent with 2018 level. Target: Sustain the number of undergraduate mentored research experiences from 2018 level. (Target Met)	Sustain the number of undergraduate mentored research experiences from 2019 level.	Sustain the number of undergraduate mentored research experiences from 2020 level.	N/A
CBRR-27 By 2020, develop a suicide risk validated assessment tool that can easily be implemented in emergency care settings. (Output)	FY 2019: Researchers validated the Computerized Adaptive Screening in a study of adolescent patients in emergency care settings. Target: Validate risk stratification approaches in emergency care settings for youth who are at risk for suicide.	Validate risk stratification approaches in emergency care settings for youth, and test clinical decision-making approaches based on risk stratification.	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
	(Target Met)			
CBRR-28 Collect and distribute human tissue samples and molecular and genetic data from human tissues to the scientific community with the purpose of supporting research on brain and behavior. (Output)	FY 2019: Brain tissue from 75 donors was obtained and tissue or data were distributed to 35 researchers. Target: Collect brain tissue from an additional 70 new donors and distribute tissue samples or data derived from tissue to 30 researchers studying mental or neurological disorders. (Target Exceeded)	Collect brain tissue from an additional 50 new donors and distribute tissue samples or data derived from tissue to 20 researchers studying mental or neurological disorders.	Collect brain tissue from an additional 50 new donors and distribute tissue samples or data derived from tissue to 20 researchers studying mental or neurological disorders.	N/A
CBRR-29 By 2020, establish an interactive consortium to facilitate efficient data collection and sharing for biomarker studies of vascular contribution to cognitive impairment and dementia (VCID). (Output)	FY 2019: Cerebrovascular Reactivity (CVR) biomarker kit protocol was finalized, staff at all four participating validation sites were trained, and sites began enrolling subjects and acquiring data. Target: Initiate multi-site validation studies for one candidate biomarker. (Target Met)	Initiate multi-site validation studies for two additional biomarker candidates.	N/A	N/A
CBRR-30 By 2024, expand the use of program-focused versus target-focused award mechanisms by NIGMS investigators. (Output)	Note: CBRR-30 will begin reporting in December 2021.	N/A	Expand NIGMS investigator participation in the Maximizing Investigators' Research Award (MIRA) program by 2 percentage points.	N/A
CTR-7 By 2022, engage a national community in the development, dissemination, and implementation of a comprehensive national	FY 2019: Stakeholders convened to share updates and discuss progress made towards implementation of the goals and objectives in the National Action Plan.	Analyze completed webinars and meetings, and brief stakeholders on Action Plan progress.	Analyze completed webinars and meetings, and brief stakeholders on Action Plan progress.	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
strategy to address the burden of chronic obstructive pulmonary disease in the US. (Output)	Target: Analyze completed webinars and meeting, and brief stakeholders on Action Plan progress. (Target Met)			
CTR-8 By 2020, improve the breadth of available metrics used to assess the number of scientists seeking research awards from NIH, and report on these expanded measures to both inform agency funding decisions, and promote transparency regarding the agency's funding strategies. (Output)	FY 2019: NIH developed a publicly available, trans-NIH report that displays Institute/Center-specific funding priorities and statistics on R01-equivalent grants. Target: By 2019, develop a central public report displaying NIH Institute/Center-specific award data on investigator-initiated R01/R37 grants. (Target Met)	By 2020, develop a central standard report to describe NIH research investments to organizations receiving R01-equivalent and Research Project Grant support according to Carnegie Classification and Funding Institute/Center.	N/A	N/A
MPO-2 Provide opportunities for enhanced leadership skills to meet the challenges of workforce management and/or individual advancements. (Output)	FY 2019: NIH examined the Management Seminar Series by conducting pre- and post-session surveys. As a result of this examination, the agenda topics covered were adjusted. The feedback generated from the series indicated that participants applied discussed concepts immediately. Target: Examine [EX] key area to enhance leadership skills - Examine the Management Seminar Series as a method for engaging and encouraging leadership in high-performing NIH employees. (Target Met)	N/A	N/A	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
MPO-3 Address diverse workforce recruitment needs to ascertain highly qualified staff to conduct or support biomedical research. (Ongoing) (Output)	FY 2019: NIH pulled and analyzed various data sets to investigate if there was an efficient method to forecast and plan recruitment cycles based on recruitment trend data across the NIH. Target: Examine [EX] key area to enhance recruitment - Examine recruitment activities to identify the most opportune times throughout the year for NIH to recruit for varying occupations. (Target Met)	Examine (EX) key area to enhance recruitment - Examine use of the shared recruitment approach, using data gathered in the first year of full-time practice, to determine if hiring goals are being met. [IM 2021/AS 2022]	Assess [AS] results of implementation - Assess process in place to identify the most opportune times throughout the year for NIH to recruit for varying occupations. [EX 2019/IM 2020]	N/A
MPO-4 Reallocate laboratory resources based on external reviews by Boards of Scientific Counselors. (Output)	FY 2019: 25 percent of Principal Investigators were reviewed resulting in approximately 25 percent of resources recommended to be reallocated. Target: Conduct BSC reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources. (Target Met)	Conduct BSC reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources.	Conduct BSC reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources.	N/A
MPO-5 Improve facility conditions in order to reach and maintain a Condition Index (CI) weighted average of 85 or above (CIwa=85). (Ongoing) (Output and Efficiency)	FY 2019: The condition of the facilities portfolio reached a CIwa of 81.91. Target: CIwa = 79.51 (Target Exceeded)	CIwa = 77.78	CIwa=77.63	N/A
MPO-7 Manage all Buildings and Facilities (B&F) line item projects so it is completed within 100 percent of the final	FY 2019: 29 of the 34 active funded projects at the Facility Project Approval Agreement level threshold were effectively managed to ensure completion within	25 Active Projects	21 Active Projects	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
approved project cost. (Ongoing) (Output)	100 percent of the final approved cost. Target: 23 Active Projects (Target Exceeded)			
MPO-8 Manage design and construction of capital facility projects funded by Building and Facilities (B&F) so that no more than 10 percent of the projects may incorporate plus or minus 10-percent adjustments of the approved scope. (Ongoing) (Output)	FY 2019: NIH managed the design and construction of 29 of the 34 funded projects without a plus or minus 10-percent adjustment to the scope. Target: 23 Active Projects (Target Exceeded)	25 Active Projects	21 Active Projects	N/A
MPO-9 Utilize performance-based contracting (PBC). (ongoing) (Output)	FY 2019: Obligated 47 percent of eligible service contracting dollars to PBC. Target: Obligate the FY 2019 goal of eligible service contracting dollars to PBC. (Target Met)	Obligate the FY 2020 goal of eligible service contracting dollars to PBC.	Obligate the FY 2021 goal of eligible service contracting dollars to PBC.	N/A
MPO-10 Conduct systematic evaluations and pilot studies to identify strategies and future needs for enhancing the quality of peer review and improving efficiency. (Output)	FY 2019: Four clusters of study sections were evaluated, with approximately 10 study sections in each cluster. Some new measures were developed during this process and added to the data considered. Target: Refine and test measures of peer review quality and efficiency. (Target Met)	N/A	N/A	N/A
MPO-11 Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-	FY 2019: Of the 109 active awards, 89 instruments (82 percent) were installed within 18 months of the	Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-	Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-	N/A

Measure[1]	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2020 Target	FY 2021 Target	FY 2021 Target +/-FY 2020 Target
supported research institutions across the nation. (Output)	Notice of Award date. Target: 75 percent of the awarded state-of-the-art instruments are acquired and installed at NIH-supported research institutions 18 months after award. (Target Exceeded)	supported research institutions across the nation 18 months after award.	supported research institutions across the nation 18 months after award.	
MPO-12 By 2020, enhance the management, oversight, and transparency of NIH-funded clinical trials through reforms to clinical trials grant applications, peer review, and tracking of awards. (Outcome)	FY 2019: NIH has implemented a policy that expects all NIH-funded clinical trials to register and submit results to ClinicalTrials.gov for all applications for grant funding, other transactions, and contracts submitted after January 18, 2017. Target: Enhance transparency of NIH-funded clinical trials by establishing an NIH policy that expects all NIH-funded clinical trials to register and submit results to ClinicalTrials.gov and by creating a more robust process for assuring compliance with the policy. (Target Met)	Deploy an enterprise-wide system for improved stewardship of NIH-funded clinical trials that will enhance the management and oversight of NIH-funded clinical trials.	N/A	N/A

[1] Performance measures do not reflect measures for the Agency for Healthcare Research and Quality (AHRQ), activities of which are proposed to be consolidated into NIH in FY 2021 as the National Institutes for Research on Safety and Quality (NIRSQ). For information on AHRQ performance measures, see the NIRSQ chapter of the NIH Congressional Justification.

GRANT AWARDS TABLE

	FY 2019 Final Allocation[3]	FY 2020 Enacted[3]	FY 2021 President's Budget[3,4]
Number of Awards	48,996	51,772	49,756
Average Award (in Whole $s)	$563,992	$563,569	$541,362
Range of Awards (in Whole $s)[1,2]	$1,000 to $29,408,845	$1,000 to $34,673,751	$1,000 to $34,343,806

[1] Award range excludes minimum values of zero to under $1,000 related primarily to no-cost extensions and co-funded actions.

[2] Award maximum estimates are based on an extrapolation from the most recent historical actual while accounting for expected budget policies applicable to each future fiscal year. The actual year-to-year fluctuations are roughly eight million dollars, plus or minus.

[3] Includes 21st Century Cures Act funding.

[4] The number of awards include 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).

NEF NARRATIVE

Budget Summary
(Dollars in Thousands)

	FY 2019[33]	FY 2020[34]	FY 2021[35]
Notification[36]	$96,000		TBD
Congressional Allocation		$225,000	

Authorizing Legislation:

Authorization…….……Section 223 of Division G of the Consolidated Appropriations Act, 2008
Allocation Method…….……..Direct Federal, Competitive Contract

Program Description and Accomplishments

The Nonrecurring Expenses Fund (NEF) permits HHS to transfer unobligated balances of expired discretionary funds from FY 2008 and subsequent years into the NEF account. Congress authorized use of the funds for capital acquisitions necessary for the operation of the Department, specifically information technology (IT) and facilities infrastructure acquisitions.

In recent years, the NEF has provided funds for critical infrastructure needs for NIH buildings, structures, and facilities, as a supplement to the regular NIH Building and Facilities (B&F) appropriations. The projects described below received NEF funds in FY 2016, FY 2017, and FY 2019.

In FY 2016, NIH received $162.1 million from the NEF for the Renovation of the E-Wing in the NIH Clinical Center Complex (CCC) - Building 10 (B10). The mission of NIH is to uncover new knowledge that leads to better health for everyone. It is a "bench to bedside" research and training mission requiring both hospital and biomedical research laboratory functions. The CCC on the Bethesda Campus is a group of facilities that collectively support this mission. B10 is a 66-year-old facility built over two years beginning in 1950 that provides clinical services, laboratories, and supporting office space. With failing infrastructure, the condition of B10 has impaired its ability to fully support its role in this mission-critical complex. Without major renovation of its infrastructure, NIH is at risk of:

[33] Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on December 4, 2018. Amount shown is notified amount, including $12,959 thousand not released to NIH.
[34] HHS has not yet notified for FY 2020. Amount shown is amount allocated to NIH from the NEF per Section 237 of Division A of the Further Consolidated Appropriations Act, 2020.
[35] HHS has not yet notified for FY 2021.
[36] Pursuant to Section 223 of Division G of the Consolidated Appropriation Act, 2008, notification is required of planned use.

- Impacting accreditation by The Joint Commission and College of Anatomical Pathologists relating to the proximity of the Anatomical Pathology area located in the adjoining F wing;
- Failing to provide the necessary functional adjacency to the existing Institutes and the Center's outpatient clinics; and
- Failing to fulfill its mission.

The renovation of the E-Wing in B10 provides major new research laboratory space replacing laboratories from aged distal wings in the complex and provides replacement of critical Clinical programs, including the Department of Transfusion Medicine. It also provides critical new state-of-the-art current Good Manufacturing Practice (cGMP) facilities to further develop Cellular Engineering initiatives for all Institutes requiring Cell Processing.

In FY 2017, NIH received $35.3 million from the NEF for R22 Refrigerant Chiller replacement. This project involves replacing one of the six existing R22 chillers, a York 5,000-ton dual steam turbine/electric driven chiller (CH-16) in Building 11, with two new 3,000-ton variable speed electric chillers and associated cooling towers. Three additional chillers (CH-17,18 and 19) will be replaced between FY 2021 and FY 2024 using B&F funds. Due to the efficiency achieved in the chilled water upgrades accomplished between 2013 and 2015, and the additional efficiency and capacity of the two new chillers, the remaining R22 chillers (CH-20 and 21) will not have to be replaced. The refrigerant removed from the demolished chillers will be used as backup for the four remaining chillers if needed.

Also in FY 2017, NIH received $16.5 million from the NEF for Emergency Generators to support the Centralized Utility Plant (CUP). The original scope of this project was to install three 2,500-kilowatt (KW) emergency generators and associated electrical gear adjacent and within the Building 11 Central Utility Plant (CUP) to feed enough power to run three steam-driven Chillers (21, 22 and 23). The Cogeneration (COGEN) Plant at NIH, which runs on natural gas, is unique in that it is believed to be the most efficient source of electrical power and steam from a stand-alone system in the world. The plant has the capability of delivering 22 megawatts (MW) of power to various substations on the Bethesda Campus, which in turn feeds the CUP. The new scope of work for this project is to direct the new emergency power generator or generators (2000 KW total) toward the startup of the COGEN plant should a loss of power occur from the local electrical utility service. In order to protect the critical mission of the NIH from disruption if the electric utility service for any reason suffers a severe voltage reduction or loss of the electrical system, the COGEN system and campus electric distribution system would automatically shut down and restart by energizing the COGEN plant through the new emergency generation system. This system will guarantee uninterrupted cooling and steam service to the most critical facilities on campus.

In FY 2019, NIH received $63.5 million from the NEF for a new CCC Utility Vault and Parking Garage. This project is for the completion of a new, 330,000 gross square foot (GSF) Utility Vault and Multi-Level Parking Garage to serve the CCC. The new Utility Vault and Parking Garage will ensure the reliability and long-term sustainability of the electrical power feeds to the 4.5 million square foot hospital and biomedical research complex and will mitigate the security risk, personal safety risk, and liability risk associated with the existing underground parking garage.

Also in FY 2019, NIH received $19.5 million from the NEF for Electrical Power Reliability at the CCC. The CCC is composed of three major structures, including the original B10, the Ambulatory Care Research Facility (ACRF), and the CRC, built in 1952, 1980, and 2005, respectively. This project consists of two major initiatives in order to achieve electrical power reliability in the CCC, including electrical vault decommissioning and upgrades to existing electrical vaults. NIH will decommission the existing vaults and fully remove existing equipment in vaults 6 and 10, including environmental requirements for removal of transformers contaminated with Polychlorinated biphenyls (PCB). NIH will replace and upgrade electrical vaults 7, 8 and 9, one vault at a time, while maintaining full functional service to the CCC in subsequent years using B&F funds.

In the FY 2020 Enacted Appropriations bill, NIH was allocated $225 million from NEF for building and facilities related investments pursuant to Section 237 of Division A of the Further Consolidated Appropriations Act, 2020 (P.L. 116-94), provided:

> Of the unobligated balances available in the ‘‘Nonrecurring Expenses Fund’’ established in section 223 of division G of Public Law 110–161, $225,000,000, in addition to any funds otherwise made available for such purpose in this or subsequent fiscal years, shall be available for buildings and facilities at the National Institutes of Health.

BUDGET REQUEST BY IC (SUMMARY TABLE)

(Dollars in Thousands)[5]	FY 2019 Final	FY 2020 Enacted[6]	FY 2021 President's Budget
NCI	$6,121,288	$6,440,438	$5,881,173
NHLBI	$3,482,377	$3,625,258	$3,298,004
NIDCR	$460,644	$477,679	$434,559
NIDDK[1]	$2,175,511	$2,265,146	$2,074,211
NINDS	$2,246,308	$2,446,577	$2,245,110
NIAID	$5,545,135	$5,876,195	$5,445,886
NIGMS[2]	$2,821,880	$2,937,218	$2,672,074
NICHD	$1,501,251	$1,556,909	$1,416,366
NEI	$793,783	$823,325	$749,003
NIEHS[3]	$850,966	$883,598	$803,835
NIA	$3,080,077	$3,545,869	$3,225,782
NIAMS	$602,918	$624,889	$568,480
NIDCD	$472,996	$490,692	$446,397
NIMH	$1,871,685	$2,042,966	$1,844,865
NIDA	$1,408,216	$1,457,724	$1,431,770
NIAAA	$525,316	$546,696	$497,346
NINR	$163,169	$172,363	$156,804
NHGRI	$575,387	$604,118	$550,116
NIBIB	$388,113	$404,638	$368,111
NIMHD	$313,211	$335,812	$305,498
NCCIH	$145,961	$151,877	$138,167
NCATS	$815,603	$832,888	$787,703
FIC	$77,921	$80,827	$73,531
NLM	$440,847	$456,911	$415,665
OD	$2,103,986	$2,404,387	$2,208,063
B&F	$199,313	$200,000	$300,000
NIRSQ[4]	---	---	$355,112
Total, NIH Program Level	**$39,183,862**	**$41,685,000**	**$38,693,631**
Special Type 1 Diabetes Research	-$150,000	-$150,000	-$150,000
PHS Program Evaluation	-$1,146,821	-$1,230,821	-$741,000
Interior Approp. (Superfund Research)	-$79,000	-$81,000	-$73,688
Patient-Centered Outcomes Research Trust Fund	---	---	-$98,452
Total, NIH Labor/HHS Budget Authority	**$37,808,041**	**$40,223,179**	**$37,630,491**

[1] Includes enacted or requested Type 1 Diabetes Research mandatory funding of $150.0 million in each of FY 2019 through FY 2021.

[2] Includes Program Evaluation financing of $1,146.8 million in FY 2019, $1,230.8 million in FY 2020, and $741.0 million in FY 2021.

[3] Includes Interior Appropriation for Superfund Research activities of $79.0 million in FY 2019, $81.0 million in FY 2020, and $73.7 million in FY 2021.

[4] Figure for FY 2021 reflects the proposed consolidation of Agency for Healthcare Research and Quality activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ). Includes Patient-Centered Outcomes Research Trust Fund (PCORTF) funding of $98.5 million.

[5] Includes funding derived by transfer from the NIH Innovation Account under the 21st Century Cures Act.

[6] Amounts for FY 2020 reflect directive transfer of $5.0 million from OD to the HHS Office of Inspector General, HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research, and $150.0 million for Type 1 Diabetes Research (enacted amount of $96.575 million through May 22, 2020 plus extension request of $53.425 million).

APPROPRIATIONS ADJUSTMENT TABLE FOR FY 2019

(Dollars in Thousands)	FY 2019 Enacted	Permissive Transfer (NIH Innovation Account)[1]	Permissive Transfer (Secretary's 1% Authority)[2]	OIG Transfer[3]	HIV/AIDS Transfer[4]	HEAL Transfer[5]	FY 2019 Final
NCI	$5,743,892	$400,000	-$19,730		-$2,874		$6,121,288
NHLBI	$3,488,335		-$11,982		$6,024		$3,482,377
NIDCR	$461,781		-$1,586		$449		$460,644
NIDDK[6]	$2,179,823		-$6,972		$2,660		$2,175,511
NINDS	$2,216,913	$57,500	-$6,756		-$4,349	-$17,000	$2,246,308
NIAID	$5,523,324		-$18,972		$35,783	$5,000	$5,545,135
NIGMS	$2,872,780		-$5,929		-$44,971		$2,821,880
NICHD	$1,506,458		-$5,175		-$32		$1,501,251
NEI	$796,536		-$2,736		-$17		$793,783
NIEHS[7]	$853,707		-$2,661		-$80		$850,966
NIA	$3,083,410		-$10,591		$7,258		$3,080,077
NIAMS	$605,065		-$2,078		-$69		$602,918
NIDCD	$474,404		-$1,630		$222		$472,996
NIMH	$1,812,796	$57,500	-$5,001		$6,390		$1,871,685
NIDA	$1,419,844		-$3,249		-$8,379		$1,408,216
NIAAA	$525,591		-$1,805		$1,530		$525,316
NINR	$162,992		-$560		$737		$163,169
NHGRI	$575,579		-$1,977		$1,785		$575,387
NIBIB	$389,464		-$1,338		-$13		$388,113
NICHD	$314,679		-$1,081		-$387		$313,211
NCCIH	$146,473		-$503		-$9		$145,961
NCATS	$806,373		-$2,770		---	$12,000	$815,603
FIC	$78,109		-$268		$80		$77,921
NLM	$441,997		-$1,518		$368		$440,847
OD	$2,632,675	-$515,000	-$6,583	-$5,000	-$2,106		$2,103,986
B&F	$200,000		-$687		---		$199,313
Total, NIH Program Level[8]	**$39,313,000**	**---**	**-$124,138**	**-$5,000**	---	**---**	**$39,183,862**
Less funds allocated from different sources:							
Mandatory Type 1 Diabetes Research	-$150,000						-$150,000
PHS Program Evaluation	-$1,146,821						-$1,146,821
Total, NIH Discretionary Budget Authority	**$38,016,179**	**---**	**-$124,138**	**-$5,000**	---	**---**	**$37,887,041**
Interior Budget Authority	-$79,000						-$79,000
Total, NIH Labor/HHS Budget Authority	**$37,937,179**	**---**	**-$124,138**	**-$5,000**	**---**	**---**	**$37,808,041**

[1]Reflects redistribution of NIH Innovation account for the 21st Century Cures Act.

[2]Identifies amounts transferred to other HHS accounts consistent with Secretary's 1% transfer authority.

[3]Reflects directive transfer of $5.0 million from OD to the HHS Office of Inspector General.

[4]Reflects HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research.

[5]Reflects transfers for opioid research under Section 225 of Division B, P.L. 115-245.

[6]Includes Type 1 Diabetes.

[7]Includes Superfund Research activity.

[8]Program level is not adjusted for 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). For information on AHRQ appropriation and adjustments, see the NIRSQ chapter of the NIH Congressional Justification.

APPROPRIATIONS ADJUSTMENT TABLE FOR FY 2020

(Dollars in Thousands)	FY 2020 Enacted	Permissive Transfer (NIH Innovation Account)[1]	OIG Transfer[2]	HIV/AIDS Transfer[3]	Requested T1D Extension[4]	FY 2020 Operating Level
NCI	$6,245,442	$195,000		-$4		$6,440,438
NHLBI	$3,624,258			$1,000		$3,625,258
NIDCR	$477,429			$250		$477,679
NIDDK[5]	$2,210,889			$832	$53,425	$2,265,146
NINDS	$2,374,687	$70,000		$1,890		$2,446,577
NIAID	$5,885,470			-$9,275		$5,876,195
NIGMS	$2,937,218			---		$2,937,218
NICHD	$1,556,879			$30		$1,556,909
NEI	$824,090			-$765		$823,325
NIEHS[6]	$883,598			---		$883,598
NIA	$3,543,673			$2,196		$3,545,869
NIAMS	$624,889			---		$624,889
NIDCD	$490,692			---		$490,692
NIMH	$1,968,374	$70,000		$4,592		$2,042,966
NIDA	$1,462,016			-$4,292		$1,457,724
NIAAA	$545,373			$1,323		$546,696
NINR	$169,113			$3,250		$172,363
NHGRI	$606,349			-$2,231		$604,118
NIBIB	$403,638			$1,000		$404,638
NIMHD	$335,812			---		$335,812
NCCIH	$151,740			$137		$151,877
NCATS	$832,888			---		$832,888
FIC	$80,760			$67		$80,827
NLM	$456,911			---		$456,911
OD	$2,744,387	-$335,000	-$5,000	---		$2,404,387
B&F	$200,000			---		$200,000
Total, NIH Program Level[7]	**$41,636,575**	**---**	**-$5,000**	---	**$53,425**	**$41,685,000**
Less funds allocated from different sources:						
Mandatory Type 1 Diabetes Research	-$96,575				-$53,425	-$150,000
PHS Program Evaluation	-$1,230,821					-$1,230,821
Total, NIH Discretionary Budget Authority	**$40,309,179**	**---**	**-$5,000**	---	---	**$40,304,179**
Interior Budget Authority	-$81,000					-$81,000
Total, NIH Labor/HHS Budget Authority	**$40,228,179**	**---**	**-$5,000**	**---**	**---**	**$40,223,179**

[1]Reflects redistribution of NIH Innovation account for the 21st Century Cures Act.

[2]Reflects directive transfer of $5.0 million from OD to the HHS Office of Inspector General.

[3]Reflects HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research.

[4]Reflects requested extension of Type 1 Diabetes Research from enacted amount of $96.575 million through May 22, 2020 to full-year level of $150.0 million.

[5] Includes Type 1 Diabetes.

[6] Includes Superfund Research activity.

[7] Program level is not adjusted for 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). For information on AHRQ appropriation and adjustments, see the NIRSQ chapter of the NIH Congressional Justification.

BUDGET MECHANISM TABLE

Budget Mechanism - Total[1,2,3]

(Dollars in Thousands)[1,2,3]	FY 2019 Final[4]		FY 2020 Enacted[5]		FY 2021 President's Budget[6]		FY 2021 +/- FY 2020	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	27,624	$14,564,519	29,508	$16,004,065	30,109	$15,631,587	601	-$372,478
Administrative Supplements[3]	*(2,341)*	437,486	*(2,300)*	501,907	*(1,517)*	277,780	*(-783)*	-224,127
Competing	11,020	$6,313,647	11,379	$6,224,996	9,505	$5,144,843	-1,874	-$1,080,153
Subtotal, RPGs	38,644	$21,315,652	40,887	$22,730,968	39,614	$21,054,209	-1,273	-$1,676,758
SBIR/STTR	2,023	1,052,394	2,140	1,118,874	1,993	1,035,570	-147	-83,304
Research Project Grants	40,667	$22,368,046	43,027	$23,849,842	41,607	$22,089,780	-1,420	-$1,760,062
Research Centers:								
Specialized/Comprehensive	998	$1,927,569	1,021	$1,895,832	926	$1,693,289	-95	-$202,542
Clinical Research	70	420,992	67	427,137	66	397,046	-1	-30,091
Biotechnology	85	142,465	79	134,917	75	122,935	-4	-11,982
Comparative Medicine	50	136,741	49	131,392	47	124,233	-2	-7,159
Research Centers in Minority Institutions	19	63,189	21	74,500	21	68,250	0	-6,250
Research Centers	1,222	$2,690,957	1,237	$2,663,777	1,135	$2,405,752	-102	-$258,024
Other Research:								
Research Careers	4,222	$790,182	4,445	$824,556	4,168	$773,975	-277	-$50,581
Cancer Education	77	20,459	101	26,890	96	25,546	-5	-1,345
Cooperative Clinical Research	257	468,112	277	461,252	232	398,865	-45	-62,387
Biomedical Research Support	131	81,134	128	80,408	119	74,706	-9	-5,702
Minority Biomedical Research Support	286	100,758	280	98,477	240	84,534	-40	-13,943
Other	2,134	1,113,725	2,277	1,171,899	2,159	1,082,833	-118	-89,066
Other Research	7,107	$2,574,370	7,508	$2,663,482	7,014	$2,440,458	-494	-$223,024
Total Research Grants	48,996	$27,633,373	51,772	$29,177,100	49,756	$26,935,990	-2,016	-$2,241,110
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,654	$170,240	3,814	$183,810	3,598	$172,660	-216	-$11,151
Institutional Awards	13,221	695,065	13,833	726,112	12,707	675,043	-1,126	-51,069
Total Research Training	16,875	$865,305	17,647	$909,923	16,305	$847,703	-1,342	-$62,220
Research & Develop. Contracts	2,455	$3,164,921	2,663	$3,349,392	2,409	$3,077,107	-254	-$272,285
(SBIR/STTR) (non-add)[3]	*(129)*	*(91,059)*	*(113)*	*(81,196)*	*(103)*	*(74,359)*	*(-10)*	*(-6,836)*
Intramural Research		$4,143,842		$4,445,880		$4,076,559		-$369,321
Res. Management & Support		1,883,396		2,014,642		1,926,132		-88,510
Res. Management & Support (SBIR Admin) (non-add)[3]		*(8,175)*		*(11,219)*		*(8,426)*		*(-2,793)*
Office of the Director - Appropriation[3,7]		*(2,103,986)*		*(2,404,387)*		*(2,208,063)*		*(-196,324)*
Office of the Director - Other		1,196,712		1,477,063		1,343,000		-134,063
ORIP (non-add)[3,7]		*(288,108)*		*(288,213)*		*(268,596)*		*(-19,617)*
Common Fund (non-add)[3,7]		*(619,166)*		*(639,111)*		*(596,467)*		*(-42,644)*
Buildings and Facilities[8]		217,313		230,000		315,000		85,000
Appropriation[3]		*(199,313)*		*(200,000)*		*(300,000)*		*(100,000)*
Type 1 Diabetes[9,10]		-150,000		-150,000		-150,000		0
Program Evaluation Financing[9]		-1,146,821		-1,230,821		-741,000		489,821
Subtotal, Labor/HHS Budget Authority		**$37,808,041**		**$40,223,179**		**$37,630,491**		**-$2,592,688**
Interior Appropriation for Superfund Research		79,000		81,000		73,688		-7,312
Total, NIH Discretionary Budget Authority		**$37,887,041**		**$40,304,179**		**$37,704,179**		**-$2,600,000**
Type 1 Diabetes[10]		150,000		150,000		150,000		0
Patient-Centered Outcomes Research Trust Fund (PCORTF)		0		0		98,452		98,452
Total, NIH Budget Authority		**$38,037,041**		**$40,454,179**		**$37,952,631**		**-$2,501,548**
Program Evaluation Financing		1,146,821		1,230,821		741,000		-489,821
Total, Program Level		**$39,183,862**		**$41,685,000**		**$38,693,631**		**-$2,991,369**

1 All Subtotal and Total numbers may not add due to rounding.
2 Includes 21st Century Cures Act funding and excludes hurricane-related supplemental financing.
3 All numbers in italics and brackets are non-add.
4 Includes $186.4 million of 21st Century Cures and $76.5 million of Type 1 Diabetes funding appropriated in FY 2019 and carried over into FY 2020. Numbers of grants and dollars for carryover are distributed by mechanism.
5 Reflects transfer of $5.0 million to the HHS OIG.
6 Includes the proposed consolidation of Agency for Healthcare Research and Quality activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ), distributed by mechanism.
7 Number of grants and dollars for the Common Fund and ORIP components of OD are distributed by mechanism and are noted here as non-adds. Office of the Director - Appropriation is the non-add total of these amounts and the funds accounted for under OD - Other.
8 Includes B&F appropriation and monies allocated ($18.0 million in FY 2019, $30.0 million in FY 2020, and $15.0 million in FY 2021) pursuant to appropriations acts provisions that funding may be used for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
9 Number of grants and dollars for mandatory Type 1 Diabetes (T1D) and NIGMS Program Evaluation financing are distributed by mechanism above; therefore, T1D and Program Evaluation financing amounts are deducted to provide subtotals for Labor/HHS Budget Authority.
10 FY 2020 reflects requested extension of Type 1 Diabetes Research from enacted amount of $96.575 million through May 22, 2020 to full-year level of $150.0 million.

BUDGET AUTHORITY BY OBJECT CLASS INCLUDING TYPE 1 DIABETES

(Dollars in Thousands)[1,2]

Object Classes	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Personnel Compensation			
Full-Time Permanent (11.1)	$1,082,734	$1,126,303	$43,569
Other Than Full-Time Permanent (11.3)	563,443	572,854	9,411
Other Personnel Compensation (11.5)	51,850	53,390	1,540
Military Personnel (11.7)	18,782	19,726	944
Special Personnel Services Payments (11.8)	206,620	207,799	1,179
Subtotal Personnel Compensation (11.9)	**$1,923,430**	**$1,980,072**	**$56,643**
Civilian Personnel Benefits (12.1)	598,272	632,163	33,891
Military Personnel Benefits (12.2)	14,523	15,137	614
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,536,224**	**$2,627,373**	**$91,148**
Travel & Transportation of Persons (21.0)	63,177	53,761	-9,417
Transportation of Things (22.0)	5,345	4,598	-746
Rental Payments to GSA (23.1)	25,576	23,790	-1,786
Rental Payments to Others (23.2)	710	646	-63
Communications, Utilities & Misc. Charges (23.3)	19,357	14,923	-4,435
Printing & Reproduction (24.0)	304	252	-52
Consultant Services (25.1)	276,756	233,281	-43,476
Other Services (25.2)	1,538,194	1,190,791	-347,403
Purchase of goods and services from government accounts (25.3)	3,763,211	3,554,610	-208,600
Operation & Maintenance of Facilities (25.4)	241,052	327,291	86,239
R&D Contracts (25.5)	1,630,542	1,526,784	-103,758
Medical Care (25.6)	36,311	32,625	-3,686
Operation & Maintenance of Equipment (25.7)	174,127	152,848	-21,279
Subsistence & Support of Persons (25.8)	470	407	-63
Subtotal Other Contractual Services (25.0)	**$7,660,663**	**$7,018,638**	**-$642,025**
Supplies & Materials (26.0)	261,434	221,016	-40,418
Equipment (31.0)	199,172	163,154	-36,018
Land and Structures (32.0)	40,810	25,267	-15,543
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	29,560,352	27,627,020	-1,933,332
Insurance Claims & Indemnities (42.0)	2	2	0
Interest & Dividends (43.0)	53	51	-2
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$37,836,955**	**$35,153,118**	**-$2,683,836**
Total Budget Authority	**$40,373,179**	**$37,780,491**	**-$2,592,688**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, supplemental financing, and Program Evaluation Financing.

[2] Figures for FY 2021 include 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 2020 do not include AHRQ.

BUDGET AUTHORITY BY OBJECT CLASS INCLUDING SSF AND MF

(Dollars in Thousands)[1,2]

Object Classes	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Personnel Compensation			
Full-Time Permanent (11.1)	$1,482,848	$1,531,018	$48,170
Other Than Full-Time Permanent (11.3)	621,105	631,179	10,074
Other Personnel Compensation (11.5)	85,861	87,792	1,931
Military Personnel (11.7)	28,375	29,574	1,198
Special Personnel Services Payments (11.8)	213,103	214,356	1,253
Subtotal Personnel Compensation (11.9)	**$2,431,292**	**$2,493,919**	**$62,627**
Civilian Personnel Benefits (12.1)	767,812	801,060	33,247
Military Personnel Benefits (12.2)	20,910	21,693	783
Benefits to Former Personnel (13.0)	1,046	1,046	0
Total Pay Costs	**$3,221,060**	**$3,317,718**	**$96,658**
Travel & Transportation of Persons (21.0)	70,334	60,753	-9,581
Transportation of Things (22.0)	7,073	6,296	-777
Rental Payments to GSA (23.1)	86,702	81,921	-4,781
Rental Payments to Others (23.2)	79,994	76,047	-3,946
Communications, Utilities & Misc. Charges (23.3)	150,164	139,558	-10,605
Printing & Reproduction (24.0)	322	270	-52
Consultant Services (25.1)	334,799	288,454	-46,345
Other Services (25.2)	2,366,292	1,968,491	-397,801
Purchase of goods and services from government accounts (25.3)	1,385,965	1,258,792	-127,173
Operation & Maintenance of Facilities (25.4)	322,692	405,137	82,445
R&D Contracts (25.5)	1,630,737	1,526,971	-103,766
Medical Care (25.6)	48,070	43,797	-4,273
Operation & Maintenance of Equipment (25.7)	360,379	329,950	-30,428
Subsistence & Support of Persons (25.8)	470	407	-63
Subtotal Other Contractual Services (25.0)	**$6,449,403**	**$5,821,998**	**-$627,405**
Supplies & Materials (26.0)	460,141	415,193	-44,948
Equipment (31.0)	245,526	207,212	-38,314
Land and Structures (32.0)	41,886	26,290	-15,596
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	29,560,352	27,627,020	-1,933,332
Insurance Claims & Indemnities (42.0)	6	6	0
Interest & Dividends (43.0)	217	209	-9
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$37,152,119**	**$34,462,773**	**-$2,689,346**
Total Budget Authority	**$40,373,179**	**$37,780,491**	**-$2,592,688**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, supplemental financing, and Program Evaluation Financing.

[2] Figures for FY 2021 include 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 2020 do not include AHRQ.

SALARIES AND EXPENSES

(Dollars in Thousands)[1,2]

Object Classes	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Personnel Compensation			
Full-Time Permanent (11.1)	$1,082,734	$1,126,303	$43,569
Other Than Full-Time Permanent (11.3)	563,443	572,854	9,411
Other Personnel Compensation (11.5)	51,850	53,390	1,540
Military Personnel (11.7)	18,782	19,726	944
Special Personnel Services Payments (11.8)	206,620	207,799	1,179
Subtotal Personnel Compensation (11.9)	**$1,923,430**	**$1,980,072**	**$56,643**
Civilian Personnel Benefits (12.1)	598,272	632,163	33,891
Military Personnel Benefits (12.2)	14,523	15,137	614
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,536,224**	**$2,627,373**	**$91,148**
Travel & Transportation of Persons (21.0)	63,177	53,761	-9,417
Transportation of Things (22.0)	5,345	4,598	-746
Rental Payments to Others (23.2)	710	646	-63
Communications, Utilities & Misc. Charges (23.3)	19,357	14,923	-4,435
Printing & Reproduction (24.0)	304	252	-52
Other Contractual Services:			
Consultant Services (25.1)	257,254	220,212	-37,042
Other Services (25.2)	1,538,194	1,190,791	-347,403
Purchase of goods and services from government accounts (25.3)[3]	2,770,609	2,490,151	-280,458
Operation & Maintenance of Facilities (25.4)	234,804	323,108	88,304
Operation & Maintenance of Equipment (25.7)	174,127	152,848	-21,279
Subsistence & Support of Persons (25.8)	470	407	-63
Subtotal Other Contractual Services	**$4,975,457**	**$4,377,517**	**-$597,940**
Supplies & Materials (26.0)	261,434	221,016	-40,418
Subtotal Non-Pay Costs	**$5,325,784**	**$4,672,714**	**-$653,070**
Total Salaries and Expense / Administrative Costs	**$7,862,008**	**$7,300,086**	**-$561,922**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, supplemental financing, and Program Evaluation Financing.

[2] Figures for FY 2021 include 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 2020 do not include AHRQ.

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

DETAIL OF FULL-TIME EQUIVALENT EMPLOYMENT (FTE)

Institutes and Centers	FY 2019 Actual	FY 2020 Estimate	FY 2021 Estimate
NCI	2,888	3,035	3,035
NHLBI	840	962	962
NIDCR	225	235	235
NIDDK	621	660	660
NINDS	496	532	532
NIAID	1,921	1,963	1,963
NIGMS	172	184	184
NICHD	525	561	561
NEI	257	273	273
NIEHS	611	662	662
NIA	417	435	435
NIAMS	217	238	238
NIDCD	129	140	140
NIMH	537	563	563
NIDA	357	382	382
NIAAA	225	238	238
NINR	89	96	96
NHGRI	321	349	349
NIBIB	93	102	102
FIC	56	61	61
NIMHD	70	68	68
NCCIH	71	73	73
NCATS	172	167	167
NLM	659	741	741
OD	792	780	780
NIRSQ[1]	---	---	238
Central Services:			
OD - CS	760	841	841
CC	1,845	1,844	1,844
CSR	410	417	417
CIT	229	257	257
ORS	516	539	539
ORF	710	707	707
Subtotal Central Services[2]	**4,470**	**4,605**	**4,605**
PHS Trust Fund (non-add) [3]	*4*	*4*	*4*
CRADA (non-add) [4]	*5*	*5*	*5*
PCOR Trust Fund[1]	---	---	7
Total	**17,231**	**18,105**	**18,350**

[1] Figures for FY 2021 reflect the proposed consolidation of Agency for Healthcare Research and Quality activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ).

[2] Reflects FTE associated with Central Services positions whose payroll costs are financed from the NIH Management Fund and the NIH Service and Supply Fund.

[3] PHS Trust Fund positions are incorporated within the IC's Direct-funded civilian FTE category and are treated as non-add values.

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

PROGRAMS PROPOSED FOR ELIMINATION

The FY 2021 request for the National Institutes of Health does not propose any programs for elimination.

PHYSICIAN'S COMPARABILITY ALLOWANCE WORKSHEET

		FY 2018 Actual	FY 2019 Actual	FY 2020 Estimate[1]	FY 2021 Estimate[2]
1) Number of Physicians Receiving PCAs		134	130	116	132
2) Number of Physicians with One-Year PCA		25	23	22	22
3) Number of Physicians with Multi-Year PCA		109	107	94	110
4) Average Annual Physician Pay (without PCA payment)		$165,495	$168,551	$166,541	$167,830
5) Average Annual PCA Payment		$19,003	$17,445	$18,741	$21,391
6) Number of Physicians Receiving PCAs by Category (non-add)	Category I Clinical Position				
	Category II Research Position	132	130	116	132
	Category III Occupational Health				
	Category IV-A Disability Evaluation				
	Category IV-B Health and Medical Admin.	2	0	0	0

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

N/A

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

Maximum annual PCA amount for category II and IV-B vary based on grade level, amount of federal service and length of the PCA agreement. The monetary range is between $4,000 and $30,000. These flexible amounts are necessary to recruit and retain the caliber of physician needed to carry out the NIH mission which directly impacts the health of the nation.

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

NIH strives to make progress recruiting and retaining qualified physicians to the Federal service. However, due to competition and more lucrative compensation in the private sector it continues to be challenging. NIH consistently has had a high turnover rate for physicians. NIH physicians require unique and specialized qualifications that make it difficult to fill vacancies.

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

In FY 2019, there were a total of 130 PCA recipients across NIH. In FY 2020 and beyond, as indicated by the decrease in recipients to-date relative to the prior year, the critical need continues to exist for highly qualified, specialized physicians to support the NIH mission. NIH still requires compensation flexibilities such as PCA to attract and retain qualified physicians.

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

N/A

[1] FY 2020 data will be approved during the FY 2021 Budget cycle.

[2] Figures for FY 2021 include 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 years prior to FY 2021 do not include AHRQ.

HISTORY OF OBLIGATIONS BY IC

(Dollars in Thousands)	FY 2012	FY 2013	FY 2014	FY 2015[1]	FY 2016[1]	FY 2017[1,7]	FY 2018[1,7,8]	FY 2019[1,7,9]	FY 2020 Enacted[1,7,10]	FY 2021 President's Budget[1,7,11]
NCI	$5,062,763	$4,789,014	$4,932,368	$4,944,593	$5,206,169	$5,636,393	$5,948,569	$5,993,599	$6,606,559	$5,881,173
NHLBI	$3,073,302	$2,903,768	$2,988,415	$2,995,546	$3,109,062	$3,209,843	$3,374,154	$3,482,237	$3,625,258	$3,298,004
NIDCR	$409,947	$387,309	$397,833	$397,672	$412,788	$424,782	$446,656	$460,613	$477,679	$434,559
NIDDK[2]	$1,943,706	$1,837,027	$1,884,377	$1,899,088	$1,963,738	$2,009,448	$1,989,700	$2,099,265	$2,465,347	$2,074,211
NINDS	$1,623,344	$1,533,793	$1,588,899	$1,604,581	$1,692,830	$1,778,684	$1,949,067	$2,413,897	$2,449,422	$2,245,110
NIAID	$4,482,369	$4,235,094	$4,401,185	$4,417,529	$4,749,884	$4,905,708	$5,262,398	$5,567,138	$5,897,413	$5,445,886
NIGMS[3]	$2,425,522	$2,293,044	$2,366,429	$2,372,199	$2,508,868	$2,646,059	$2,780,954	$2,821,806	$2,937,218	$2,672,074
NICHD	$1,318,943	$1,246,140	$1,283,314	$1,286,797	$1,338,280	$1,376,541	$1,449,613	$1,508,603	$1,556,909	$1,416,366
NEI	$701,407	$657,055	$675,551	$676,726	$707,002	$731,203	$770,483	$793,767	$823,325	$749,003
NIEHS[4]	$763,225	$721,331	$743,002	$745,533	$769,730	$789,860	$826,646	$850,793	$883,598	$803,835
NIA	$1,120,391	$1,040,565	$1,171,656	$1,197,459	$1,596,005	$2,048,792	$2,571,438	$3,080,043	$3,545,869	$3,225,782
NIAMS	$534,791	$505,206	$520,314	$521,480	$540,874	$556,568	$585,240	$602,907	$624,889	$568,480
NIDCD	$415,500	$392,540	$404,237	$405,168	$422,311	$435,877	$458,876	$472,988	$490,692	$446,397
NIMH	$1,477,516	$1,396,006	$1,419,632	$1,433,603	$1,516,325	$1,604,624	$1,754,423	$1,869,653	$2,044,988	$1,844,865
NIDA	$1,051,410	$993,404	$1,017,957	$1,015,695	$1,048,971	$1,070,813	$1,161,149	$1,621,334	$1,457,724	$1,431,770
NIAAA	$458,665	$433,247	$446,282	$447,152	$466,713	$482,449	$508,398	$525,282	$546,696	$497,346
NINR	$144,500	$136,516	$140,553	$140,837	$145,701	$149,930	$157,633	$163,165	$172,363	$156,804
NHGRI	$512,258	$483,650	$498,076	$498,648	$512,486	$528,316	$556,741	$575,361	$604,118	$550,116
NIBIB	$337,728	$319,062	$326,989	$327,223	$342,997	$356,971	$376,700	$388,079	$404,638	$368,111
NIMHD	$275,927	$260,671	$268,439	$270,480	$280,264	$287,640	$304,372	$313,195	$335,812	$305,498
NCCIH	$127,820	$120,767	$124,368	$124,046	$129,760	$134,373	$141,667	$145,933	$151,877	$138,167
NCATS	$574,297	$542,598	$633,571	$632,629	$684,366	$704,248	$754,080	$847,430	$832,888	$787,703
FIC	$69,493	$65,627	$67,575	$67,576	$69,996	$71,813	$75,534	$77,894	$80,827	$73,531
NLM[5]	$373,087	$325,088	$334,383	$336,653	$393,074	$406,250	$424,789	$441,645	$456,911	$415,665
ORIP	$303,525	$290,042	$294,486	$294,662	$295,783	$279,130	$289,205	$288,096	$288,213	$268,596
Common Fund	$544,930	$513,461	$531,146	$545,607	$675,628	$695,430	$600,707	$619,166	$639,111	$596,467
OD - Other	$608,713	$608,584	$477,293	$573,328	$599,263	$714,058	$1,016,632	$1,185,155	$1,536,353	$1,343,000
B&F	$125,308	$106,676	$88,880	$123,464	$79,883	$113,415	$106,434	$211,107	$200,000	$300,000
NIRSQ[6]	---	---	---	---	---	---	---	---	---	$256,660
PCORTF	---	---	---	---	---	---	---	---	---	$98,452
Total, NIH Program Level	**$30,860,387**	**$29,137,284**	**$30,027,205**	**$30,295,974**	**$32,258,751**	**$34,149,217**	**$36,642,258**	**$39,420,151**	**$42,136,697**	**$38,693,631**
Less funds allocated from different sources:										
Mandatory - Special type 1 Diabetes Research	-$150,000	-$142,350	-$139,200	-$150,000	-$150,000	-$139,650	-$26,292	-$73,923	-$350,201	-$150,000
PHS Program Evaluation	-$8,200	-$8,200	-$8,200	-$715,000	-$780,000	-$824,443	-$922,871	-$1,146,821	-$1,230,821	-$741,000
PCORTF	---	---	---	---	---	---	---	---	---	-$98,452
Total, NIH Discretionary Budget Authority	**$30,702,187**	**$28,986,734**	**$29,879,805**	**$29,430,974**	**$31,328,751**	**$33,185,124**	**$35,693,095**	**$38,199,407**	**$40,555,675**	**$37,704,179**
Interior Budget Authority	-$78,928	-$74,864	-$77,345	-$77,349	-$77,252	-$77,337	-$77,342	-$78,988	-$81,000	-$73,688
Total, NIH Labor/HHS Budget Authority	**$30,623,259**	**$28,911,870**	**$29,802,460**	**$29,353,625**	**$31,251,499**	**$33,107,787**	**$33,021,788**	**$38,120,419**	**$40,474,675**	**$37,630,491**

[1] Excludes Ebola, Zika and other supplemental funding or transfers.

[2] Includes Special type 1 Diabetes Research mandatory account funding (through FY 2021). FY 2020 includes carryover of $123,707,707 from FY 2018 and $76,493,143 from FY 2019.

[3] Includes PHS Program Evaluation financing of $715,000,000 in FY 2015, $780,000,000 in FY 2016, $824,443,000 in FY 2017, $922,871,000 in FY 2018, $1,146,821,000 in FY 2019, $1,230,821,000 in FY 2020 and $741,000,000 in FY 2021.

[4] Includes Interior Appropriation allocation for Superfund Research activities.

[5] Includes PHS Program Evaluation financing of $8,200,000 for years before FY 2015.

[6] The FY 2021 Budget proposes to consolidate Agency for Healthcare Research and Quality (AHRQ) activities into NIH as the National Institute for Research on Safety and Quality (NIRSQ). Figures for years prior to FY 2021 do not include AHRQ.

[7] Includes funds under the 21st Century Cures Act.

[8] Includes obligations of $60,647,563 of 21st Century Cures carryover from FY 2017.

[9] Includes obligations of $429,883,740 of FY 2018 Opioids carryover in various ICs and $42,852,637 of 21st Century Cures carryover from FY 2017 and FY 2018 in various ICs and $415,197 of T1D carryover.

[10] Includes CURES carryover obligations of $230,278,992

[11] Amounts represent estimated or requested budget authority as opposed to obligations displayed in historical years.

HISTORY OF OBLIGATIONS BY TOTAL MECHANISM

(Dollars in Thousands)[1]	FY 2012 Actual	FY 2013 Actual	FY 2014 Actual	FY 2015 Actual[4]	FY 2016 Actual[4]	FY 2017 Actual[4]	FY 2018 Actual[4,5]	FY 2019 Actual[4,6]	FY 2020 Enacted[4,7]	FY 2021 President's Budget[4,8,9]
Research Project Grants	$16,550,486	$15,445,463	$16,168,246	$16,441,843	$17,839,691	$19,105,304	$20,756,893	$22,493,313	$24,113,572	$22,089,780
Research Centers	$3,040,375	$2,708,744	$2,723,203	$2,663,064	$2,573,774	$2,536,308	$2,581,750	$2,680,161	$2,673,878	$2,405,752
Other Research	$1,808,138	$1,783,481	$1,846,841	$1,802,719	$2,019,736	$2,181,261	$2,371,164	$2,698,036	$2,669,208	$2,440,458
Subtotal, Research Grants	**$21,398,999**	**$19,937,688**	**$20,738,290**	**$20,907,625**	**$22,433,201**	**$23,822,873**	**$25,709,807**	**$27,871,510**	**$29,456,658**	**$26,935,990**
Research Training	$761,934	$733,524	$738,429	$758,017	$803,869	$827,397	$855,844	$865,305	$909,923	$847,703
R & D Contracts	$2,937,188	$2,927,077	$2,990,037	$2,826,971	$2,913,224	$3,046,759	$3,072,406	$3,124,750	$3,452,242	$3,077,107
Intramural Research	$3,401,506	$3,247,193	$3,373,601	$3,409,362	$3,682,831	$3,780,181	$3,972,054	$4,179,250	$4,455,880	$4,076,559
Res. Mgt. & Support	$1,530,874	$1,485,575	$1,527,131	$1,619,784	$1,653,230	$1,747,406	$1,813,738	$1,886,087	$2,014,642	$1,926,132
Office of the Director[2]	$609,530	$608,584	$477,293	$573,328	$599,263	$701,864	$1,016,633	$1,185,155	$1,536,353	$1,343,000
Subtotal	**$30,640,031**	**$28,939,641**	**$29,844,781**	**$30,095,088**	**$32,085,618**	**$33,928,465**	**$36,440,482**	**$39,112,057**	**$41,825,698**	**$38,206,491**
Buildings & Facilities[3]	$133,228	$114,580	$96,880	$123,464	$95,883	$143,415	$124,434	$229,107	$230,000	$315,000
Interior- Superfund	$78,928	$74,864	$77,345	$77,332	$77,252	$77,337	$77,342	$78,988	$81,000	$73,688
PCORTF	---	---	---	---	---	---	---	---	---	$98,452
Total	**$30,852,187**	**$29,129,085**	**$30,019,005**	**$30,295,884**	**$32,258,753**	**$34,149,217**	**$36,642,258**	**$39,420,151**	**$42,136,698**	**$38,693,631**

[1] Obligations for actual years exclude lapse. Amounts for all years include Special Type 1 Diabetes. All Subtotal and Total numbers may not add due to rounding. FY 2017 through FY 2021 includes 21st Century Cures Act funding. All years exclude Ebola-related and supplemental financing.

[2] Excludes obligations for the Common Fund and the Office of Research Infrastructure Programs, which are distributed by mechanism.

[3] Includes B&F appropriation and monies allocated ($18,000,000 in FY 2018, $18,000,000 in FY 2019, $30,000,000 in FY 2020 and $15,000,000 in FY 2021) pursuant to appropriations acts provisions that funding may be used for facilities repairs and improvements at the NCI Federally funded Research and Development Center in Frederick,

[4] Includes Program Evaluation Financing resources of $715,000,000 in FY 2015, $780,000,000 in FY 2016, $824,443,000 in FY 2017, $922,871,000 in FY 2018, $1,146,821,000 in FY 2019, $1,230,821,000 in FY 2020 and $741,000,000 in FY 2021.

[5] Includes obligations of $60,647,563 of 21st Century Cures Act funding which was appropriated in FY 2017, but carried over into FY 2018.

[6] Includes obligations of $42,852,637 of 21st Century Cures Act funding which was appropriated in FY 2017 and FY 2018, but carried over into FY 2019. Similarly, includes $429,883,740 of Opioids funding and $415,917 of Type 1 Diabetes funding carried over from FY 2018. Obligations of carryover funding are distributed by mechanism.

[7] Includes estimated obligations of $230,278,992 of 21st Century Cures Act funding which was appropriated in FY 2017 through FY 2019, but carried over into FY 2020. Similarly, includes $200,200,850 of Type 1 Diabetes funding carried over from FY 2018 and FY 2019. Obligations of carryover funding are distributed by mechanism.

[8] Figures for FY 2021 include the proposed consolidation of Agency for Healthcare Research and Quality (AHRQ) activities into NIH as National Institute for Research on Safety and Quality (NIRSQ). Figures for years prior to FY 2021 do not include AHRQ.

[9] FY 2021 figures based on requested budget authority.

STATISTICAL DATA: DIRECT AND INDIRECT COSTS AWARDED

(Dollars in Thousands)	Direct Cost Awarded	Indirect Cost Awarded	Percent of Total		Percent Change	
			Direct Cost Awarded	Indirect Cost Awarded	Direct Cost Awarded	Indirect Cost Awarded
FY 2009	$15,683,872	$6,027,543	72.2%	27.8%	2.5%	2.1%
FY 2010	$16,040,991	$6,193,567	72.1%	27.9%	2.3%	2.8%
FY 2011	$15,849,082	$6,173,769	72.0%	28.0%	-1.2%	-0.3%
FY 2012	$15,978,032	$6,182,900	72.1%	27.9%	0.8%	0.2%
FY 2013	$14,915,599	$5,755,617	72.2%	27.8%	-6.7%	-6.9%
FY 2014	$15,568,553	$5,908,275	72.5%	27.5%	4.4%	2.7%
FY 2015	$15,645,282	$6,020,843	72.2%	27.8%	0.5%	1.9%
FY 2016	$16,791,158	$6,445,133	72.3%	27.7%	7.3%	7.1%
FY 2017[1]	$17,799,515	$6,838,801	72.2%	27.8%	6.0%	6.1%
FY 2018[1,3]	$19,599,758	$7,481,452	72.4%	27.6%	10.1%	9.4%
FY 2019 Final[1,4]	$20,544,931	$7,953,747	72.1%	27.9%	4.8%	6.3%
FY 2020 Enacted[1]	$21,687,098	$8,399,925	72.1%	27.9%	5.6%	5.6%
FY 2021 President's Budget[1,2]	$20,032,326	$7,751,367	72.1%	27.9%	-7.6%	-7.7%

Note: Data for fiscal years 2020 and later represent estimates and will change as actual data are received.

[1] Includes 21st Century Cures Act funding.

[2] The figures include 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).

[3] Figures are revised to reflect updated estimates of awards from FY 2018 budget authority carried into FY 2019.

[4] Figures include estimates of awards from FY 2019 budget authority carried into FY 2020.

RPGS – TOTAL NUMBER OF AWARDS AND FUNDING

(Dollars in Thousands)	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017 Final[3]	FY 2018 Final[3,5]	FY 2019 Final[3,6]	FY 2020 Enacted[3]	FY 2021 President's Budget[3,4]
No. of Awards:										
Competing	8,986	8,234	9,168	9,540	10,364	10,123	11,116	11,020	11,379	9,505
Noncompeting	25,631	25,140	23,504	23,261	23,528	24,638	25,780	27,624	29,508	30,109
Subtotal	34,617	33,374	32,672	32,801	33,892	34,761	36,896	38,644	40,887	39,614
SBIR/STTR	1,642	1,466	1,660	1,578	1,689	1,807	2,034	2,023	2,140	1,993
Total	**36,259**	**34,840**	**34,332**	**34,379**	**35,581**	**36,568**	**38,930**	**40,667**	**43,027**	**41,607**
Average Annual Cost:										
Competing RPGs	$421	$418	$489	$452	$484	$522	$527	$573	$547	$541
Total RPGs[1]	459	444	474	479	502	523	546	552	556	531
Percent Change in Average Cost from Prior Year[2]										
Competing RPGs	-1.5%	-0.8%	17.0%	-7.5%	7.2%	7.8%	1.0%	8.7%	-4.5%	-1.1%
Total RPGs[1]	1.4%	-3.3%	6.7%	1.2%	4.8%	4.0%	4.4%	1.1%	0.8%	-4.4%
Average Length of Award in Years	**3.5**	**3.5**	**3.5**	**3.5**	**3.6**	**3.6**	**3.6**	**3.6**	**3.6**	**3.6**

NOTE: Includes awards supported by the Common Fund program (for all years) and the Type 1 Diabetes mandatory account.

[1] Includes Noncompeting RPGs and Administrative Supplements. Excludes SBIR/STTR awards.

[2] Based on average costs in whole dollars.

[3] Includes 21st Century Cures Act funding.

[4] Figures include 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).

[5] Figures are revised to reflect updated estimates of awards from FY 2018 budget authority carried into FY 2019.

[6] Figures include estimates of awards from FY 2019 budget authority carried into FY 2020.

RPGS – SUCCESS RATES

INSTITUTES & CENTERS[*,1,2]	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017 Final[6]	FY 2018 Final[6,8]	FY 2019 Final[6,9]	FY 2020 Enacted[6]	FY 2021 President's Budget[6,7]
NCI	13.6%	13.7%	14.1%	13.0%	12.0%	11.7%	11.3%	11.9%	12.8%	12.7%
NHLBI	14.7%	16.9%	18.2%	21.9%	24.2%	23.5%	25.1%	22.3%	22.8%	19.8%
NIDCR	21.2%	19.9%	21.5%	22.0%	19.9%	17.8%	22.2%	23.8%	23.0%	18.5%
NIDDK	19.8%	21.0%	22.9%	20.3%	20.1%	17.8%	21.6%	20.3%	24.7%	19.0%
NINDS	19.5%	19.8%	18.7%	20.5%	19.8%	17.7%	22.4%	20.4%	22.7%	14.1%
NIAID	23.2%	18.8%	22.0%	21.5%	23.8%	19.1%	22.9%	22.1%	23.1%	17.1%
NIGMS	24.4%	19.9%	24.8%	29.6%	29.6%	30.6%	29.2%	32.6%	30.0%	24.1%
NICHD	12.5%	10.8%	12.5%	11.5%	13.2%	16.1%	18.4%	19.5%	19.9%	18.1%
NEI	29.8%	23.7%	26.7%	21.4%	25.7%	24.9%	26.7%	28.4%	27.1%	24.2%
NIEHS	14.3%	15.3%	15.0%	14.7%	14.2%	15.0%	17.1%	14.8%	17.0%	17.6%
NIA	15.5%	13.6%	15.9%	17.7%	22.8%	26.6%	28.9%	29.2%	23.4%	16.0%
NIAMS	15.6%	15.9%	18.1%	16.7%	16.0%	17.0%	16.7%	17.1%	15.6%	14.0%
NIDCD	26.6%	22.5%	25.8%	24.9%	26.7%	24.4%	27.1%	25.2%	22.8%	21.0%
NIMH	21.6%	18.7%	19.4%	20.4%	22.9%	20.9%	22.2%	24.8%	26.3%	17.4%
NIDA	21.2%	19.5%	18.0%	19.6%	15.4%	19.7%	19.4%	17.5%	16.9%	15.0%
NIAAA	18.4%	19.5%	19.2%	16.4%	18.8%	22.0%	26.7%	20.9%	22.1%	16.3%
NINR	13.0%	9.1%	11.6%	8.0%	9.0%	8.9%	10.3%	9.3%	8.4%	8.3%
NHGRI	23.9%	20.5%	17.7%	18.8%	25.6%	23.9%	28.0%	19.2%	23.4%	31.4%
NIBIB	12.1%	13.7%	13.1%	12.0%	14.6%	13.0%	16.8%	18.3%	20.2%	14.0%
NIMHD	9.9%	4.3%	11.9%	13.7%	19.3%	21.5%	10.7%	7.5%	5.4%	9.8%
NCCIH[3]	9.5%	11.6%	8.7%	10.8%	13.9%	16.7%	20.3%	12.5%	13.9%	13.4%
NCATS[4]	0.0%	N/A	16.7%	66.7%	27.7%	21.8%	36.4%	20.7%	21.9%	9.1%
FIC	16.0%	14.6%	9.1%	9.7%	29.5%	10.8%	19.5%	20.6%	27.8%	25.4%
NLM	12.8%	12.3%	19.4%	19.8%	13.0%	14.9%	17.7%	18.4%	12.9%	13.8%
ORIP & SEPA[5]	18.6%	20.0%	19.6%	21.5%	18.8%	16.5%	17.8%	34.2%	18.4%	17.3%
Common Fund	8.0%	9.2%	10.0%	12.1%	12.6%	11.8%	10.9%	11.0%	10.7%	9.5%
NIH	**17.5%**	**16.7%**	**18.0%**	**18.3%**	**19.1%**	**18.7%**	**20.3%**	**20.1%**	**20.3%**	**16.5%**
NIRSQ	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	25.0%
NIH	**17.5%**	**16.7%**	**18.0%**	**18.3%**	**19.1%**	**18.7%**	**20.3%**	**20.1%**	**20.3%**	**16.5%**

* Success Rates identified in FY 2020 and FY 2021 are estimates, and will change as applications are received and selected for funding.

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

[2] Includes Special type 1 Diabetes Research program administered by NIDDK. Excludes NIEHS Superfund Research and OD Other awards.

[3] The National Center for Complementary and Alternative Medicine (NCCAM) was renamed in December 2014 to the National Center for Complementary and Integrative Health (NCCIH).

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

[5] The SEPA program transitioned to NIGMS in FY 2017 from the NIH Office of Research Infrastructure Program (ORIP).

[6] Includes 21st Century Cures Act funding.

[7] Figures include 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).

[8] Figures are revised to reflect updated estimates of awards from FY 2018 budget authority carried into FY 2019.

[9] Figures include estimates of awards from FY 2019 budget authority carried into FY 2020.

TOTAL R01 EQUIVALENT DATA FOR FIRST TIME AND ESTABLISHED INVESTIGATORS

R01 Equivalent Grants[1,2,3,4,5]	FY 2019 Final[7]	FY 2020 Enacted	FY 2021 President's Budget[6]
Applications			
Received	35,085	36,821	39,046
Funded	7,356	7,939	6,838
Total Investigators			
Received	31,170	32,560	34,559
Funded	8,846	9,592	8,327
Established Investigators			
Received	19,202	19,948	21,009
Funded	6,232	6,770	5,848
First-time Investigators			
Received	11,968	12,612	13,550
Funded	2,614	2,822	2,479

[1] Grant data is based on linear extrapolation of five years of latest actual data.

[2] Excludes applications and awards associated with reimbursable agreements and Superfund Research.

[3] Estimates for received applications reflect consolidations of Institute/Center validated refinements to linear extrapolation of five years of latest actual data.

[4] Includes 21st Century Cures Act funding.

[5] R01 Equivalent Grants form a subset of all RPG awards, comprising roughly 63% of Applications, 69% of Total Investigators, 78% of Established Investigators and 56% of First-time Applicants.

[6] Figures include 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).

[7] Figures include estimates of awards from FY 2019 budget authority carried into FY 2020.

COMPETING RPGS BY LENGTH OF AWARD

(Dollars in Thousands)	FY 2019 Final[4]		FY 2020 Enacted		FY 2021 President's Budget[3]	
	No.	Amount	No.	Amount	No.	Amount
Competing RPGs:[1,2]						
One-Year Awards	1,263	$1,440,681	1,105	$1,204,232	923	$995,275
Two-Year Awards	2,629	$611,336	2,835	$654,513	2,368	$540,942
Three-Year Awards	497	$332,872	571	$339,788	477	$280,829
Four-Year Awards	1,997	$1,092,568	2,155	$1,170,825	1,800	$967,665
Five or More Year Awards	4,634	$2,836,190	4,713	$2,855,638	3,937	$2,360,132
Total Competing RPGs	11,020	$6,313,647	11,379	$6,224,996	9,505	$5,144,843

[1] The distribution of awards with durations of 1, 2, 3, 4 and 5+ years is based on historical data.

[2] Includes 21st Century Cures Act funding.

[3] Figures include 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).

[4] Figures include estimates of awards from FY 2019 budget authority carried into FY 2020.

NON-COMPETING COMMITMENTS

(Dollars in Thousands)	FY 2019 Final[4,6]	FY 2020 Enacted[4]	FY 2021 President's Budget[4,5]
Research Project Grants (RPGs)			
Noncompeting:			
Number	27,624	29,508	30,109
Amount	$14,564,519	$16,004,065	$15,631,587
Administrative Supp	$437,486	$501,907	$277,780
Competing:			
Number	11,020	11,379	9,505
Amount	$6,313,647	$6,224,996	$5,144,843
SBIR/STTR:			
Number	2,023	2,140	1,993
Noncompeting	999	832	790
Amount[1]	$1,052,394	$1,118,874	$1,035,570
Noncompeting	$519,830	$435,154	$410,505
Subtotal, RPGs:			
Number	40,667	43,027	41,607
Amount	$22,368,046	$23,849,842	$22,089,780
Research Centers:			
Number	1,222	1,237	1,135
Noncompeting	919	944	978
Amount	$2,690,957	$2,663,777	$2,405,752
Noncompeting	$2,023,238	$2,032,765	$2,072,174
Other Research:			
Number	7,107	7,508	7,014
Noncompeting	4,646	5,365	6,110
Amount	$2,574,370	$2,663,482	$2,440,458
Noncompeting	$1,682,938	$1,903,205	$2,125,829
Training:			
FTTPs	16,875	17,647	16,305
Noncompeting	12,723	13,899	13,529
Amount	$865,305	$909,923	$847,703
Noncompeting	$652,389	$716,664	$703,357
Total Extramural Research[2]	**$28,498,678**	**$30,087,023**	**$27,783,693**
Noncompeting Number/FTTPs	46,911	50,548	51,516
Competing Number/FTTPs	18,960	18,871	14,545
Noncompeting Amount	$19,880,400	$21,593,760	$21,221,232
Competing Amount	$8,618,278	$8,493,263	$6,562,461
Total Percent Change	**5.2%**	**5.6%**	**-7.7%**
Total Discretionary Budget Authority[3]	**$39,033,862**	**$41,535,000**	**$38,445,179**
Percent Change	**5.3%**	**6.4%**	**-7.4%**

[1] The 3.65% combined SBIR/STTR program threshold is achieved in FY 2019 and sustained in subsequent years.

[2] Includes both grants and FTTPs for Noncompeting and Competing numbers

[3] Includes Labor/HHS appropriations, the Interior Superfund Research account, 21st Century Cures Act funding, as well as Program Evaluation financing resources. Excludes mandatory accounts such as Type 1 Diabetes.

[4] Includes 21st Century Cures Act funding.

[5] Figures include 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).

[6] Figures include estimates of awards from FY 2019 budget authority carried into FY 2020.

MF GENERAL STATEMENT

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

MF BUDGET AUTHORITY BY ACTIVITY

Budget Authority by Activity
(Dollars in thousands)

	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Detail:								
Clinical Center	1,845	$555,873	1,844	$588,763	1,844	$588,763	0	$0
Center for Scientific Review	410	143,622	417	146,126	417	138,820	0	(7,306)
Office of Research Services, Development & Operations and Administrative services	258	76,634	270	79,270	270	75,306	0	(3,964)
TOTAL	**2,513**	**$776,129**	**2,531**	**$814,159**	**2,531**	**$802,889**	**0**	**($11,270)**

MF BUDGET AUTHORITY BY OBJECT CLASS

(Dollars in thousands)

		FY 2020 Enacted	FY 2021 President's Budget	Increase or Decrease
Total compensable workyears:				
	Full-time employment	2,531	2,531	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$190	$191	1
	Average GM/GS grade	11.1	11.1	0
	Average GM/GS salary	$102	$103	1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$108	$109	1
	Average salary of ungraded positions	98	99	1
	OBJECT CLASSES	**FY 2020 Enacted**	**FY 2021 President's Budget**	**Increase or Decrease**
	Personnel Compensation:			
11.1	Full-time permanent	$200,654	$202,961	$2,308
11.3	Other than full-time permanent	48,829	49,390	562
11.5	Other personnel compensation	22,765	23,027	262
11.7	Military personnel	6,630	6,805	176
11.8	Special personnel services payments	6,335	6,408	73
	Total, Personnel Compensation	**285,212**	**288,591**	**3,379**
12.0	Personnel benefits	89,367	89,027	(340)
12.2	Military personnel benefits	4,765	4,891	126
13.0	Benefits for former personnel	61	61	0
	Subtotal, Pay Costs	**379,405**	**382,571**	**3,166**
21.0	Travel and transportation of persons	3,801	3,801	0
22.0	Transportation of things	1,091	1,091	0
23.1	Rental payments to GSA	9	9	0
23.2	Rental payments to others	39	39	0
23.3	Communications, utilities and miscellaneous charges	4,871	4,871	0
24.0	Printing and reproduction	15	15	0
25.1	Consulting services	24,926	23,680	(1,246)
25.2	Other services	138,629	131,697	(6,931)
25.3	Purchase of goods and services from government accounts	91,484	88,195	(3,289)
25.4	Operation and maintenance of facilities	4,202	4,202	0
25.5	Research and development contracts	17	17	0
25.6	Medical care	11,048	10,496	(552)
25.7	Operation and maintenance of equipment	23,296	22,131	(1,165)
25.8	Subsistence and support of persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**293,603**	**280,418**	**(13,184)**
26.0	Supplies and materials	106,253	106,253	0
31.0	Equipment	25,029	23,778	(1,251)
32.0	Land and structures	8	8	0
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	0	0	0
42.0	Insurance claims and indemnities	1	1	0
43.0	Interest and dividends	34	34	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**434,755**	**420,319**	**(14,436)**
	Total Budget Authority by Object	**814,159**	**802,889**	**(11,270)**

MF DETAIL OF POSITIONS

GRADE	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Total, ES Positions	4	4	4
Total, ES Salary	$742,807	$759,908	$763,707
GM/GS-15	110	113	114
GM/GS-14	322	328	333
GM/GS-13	324	327	327
GS-12	490	492	492
GS-11	452	454	454
GS-10	35	35	35
GS-9	122	131	131
GS-8	86	92	92
GS-7	210	221	221
GS-6	47	48	48
GS-5	20	20	20
GS-4	8	9	9
GS-3	10	11	11
GS-2	3	3	3
GS-1	1	1	1
Subtotal	2,240	2,285	2,291
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	12	12	12
Senior Grade	17	17	17
Full Grade	14	14	14
Senior Assistant Grade	16	16	16
Assistant Grade	1	1	1
Subtotal	60	60	60
Ungraded	329	334	334
Total permanent positions	2,274	2,284	2,284
Total positions, end of year	2,633	2,683	2,689
Total full-time equivalent (FTE) employment, end of year	2,513	2,531	2,531
Average ES salary	185,702	189,977	190,927
Average GM/GS grade	11.2	11.1	11.1
Average GM/GS salary	99,107	101,572	102,852

SSF GENERAL STATEMENT

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

SSF BUDGET AUTHORITY BY ACTIVITY

Budget Authority by Activity
(Dollars in thousands)

	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Detail:								
Research Support and Administrative (OD & includes CIF, ORS)	1,018	$1,102,287	1,110	$1,132,048	1,110	$1,075,447	0	($56,601)
Office of Research Facilities Development & Operations (ORF)	710	544,952	707	559,666	707	531,682	0	(27,984)
Information Technology (CIT)	229	354,853	257	364,434	257	346,212	0	(18,222)
TOTAL	**1,957**	**$2,002,092**	**2,074**	**$2,056,148**	**2,074**	**$1,953,341**	**0**	**($102,807)**

SSF BUDGET AUTHORITY BY OBJECT

(Dollars in Thousands)

		FY 2020 Enacted	FY 2021 President's Budget	Increase or Decrease
Total compensable workyears:				
	Full-time employment	2,074	2,074	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$191	$192	1
	Average GM/GS grade	12.0	12.0	0
	Average GM/GS salary	$110	$111	1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$103	$104	1
	Average salary of ungraded positions	140	141	1
	OBJECT CLASSES	**FY 2020 Enacted**	**FY 2021 President's Budget**	**Increase or Decrease**
	Personnel Compensation:			
11.1	Full-time permanent	$199,460	$201,754	$2,294
11.3	Other than full-time permanent	8,834	8,935	102
11.5	Other personnel compensation	11,245	11,375	129
11.7	Military personnel	2,964	3,043	79
11.8	Special personnel services payments	148	149	2
	Total, Personnel Compensation	**222,650**	**225,255**	**2,605**
12.0	Personnel benefits	80,174	79,869	(305)
12.2	Military personnel benefits	1,622	1,665	43
13.0	Benefits for former personnel	985	985	0
	Subtotal, Pay Costs	**305,431**	**307,774**	**2,343**
21.0	Travel and transportation of persons	3,355	3,191	(164)
22.0	Transportation of things	637	606	(31)
23.1	Rental payments to GSA	61,117	58,122	(2,995)
23.2	Rental payments to others	79,245	75,362	(3,883)
23.3	Communications, utilities and miscellaneous charges	125,936	119,765	(6,171)
24.0	Printing and reproduction	3	3	(0)
25.1	Consulting services	33,116	31,493	(1,623)
25.2	Other services	689,469	646,003	(43,467)
25.3	Purchase of goods and services from government accounts			0
25.3	Rent Portion of SSF (Rent paid out of OC 81)	47,994	45,642	
25.3	OC 81 Other than Rent	31,415	29,876	
25.3	OC 25.93 Management Fund	45,232	43,016	
25.3	Other	276,936	253,684	
25.4	Operation and maintenance of facilities	77,438	73,644	(3,794)
25.5	Research and development contracts	178	169	(9)
25.6	Medical care	711	676	(35)
25.7	Operation and maintenance of equipment	162,956	154,971	(7,985)
25.8	Subsistence and support of persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**1,365,445**	**1,279,173**	**(86,272)**
26.0	Supplies and materials	92,454	87,924	(4,530)
31.0	Equipment	21,325	20,280	(1,045)
32.0	Land and structures	1,068	1,015	(52)
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	0	0	0
42.0	Insurance claims and indemnities	3	3	(0)
43.0	Interest and dividends	130	124	(6)
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**1,750,717**	**1,645,566**	**(105,151)**
	Total Budget Authority by Object	**2,056,148**	**1,953,341**	**(102,807)**

SSF DETAIL OF POSITIONS

GRADE	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Total, ES Positions	8	8	8
Total, ES Salary	$1,519,561	$1,530,671	$1,538,579
GM/GS-15	95	105	107
GM/GS-14	304	323	326
GM/GS-13	598	630	632
GS-12	310	324	322
GS-11	100	105	105
GS-10	6	6	6
GS-9	87	96	96
GS-8	25	25	25
GS-7	61	65	65
GS-6	10	10	10
GS-5	10	12	12
GS-4	21	21	21
GS-3	19	19	19
GS-2	8	8	8
GS-1	12	12	12
Subtotal	1,666	1,761	1,766
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	7	7	7
Senior Grade	6	7	7
Full Grade	13	14	14
Senior Assistant Grade	4	4	4
Assistant Grade	1	1	1
Subtotal	31	33	33
Ungraded	321	335	335
Total permanent positions	1,920	2,034	2,039
Total positions, end of year	2,026	2,137	2,142
Total full-time equivalent (FTE) employment, end of year	1,957	2,074	2,074
Average ES salary	189,945	191,334	192,322
Average GM/GS grade	12.0	12.0	12.0
Average GM/GS salary	108,670	109,768	110,912

GOOD ACCOUNTING OBLIGATION IN GOVERNMENT ACT (GAO-IG ACT) REPORT

The information below addresses the requirements of the Good Accounting Obligation in Government Act (GAO-IG Act; Public Law 115-414) to provide a report identifying each public recommendation issued by the Government Accountability Office (GAO) and federal Offices of Inspectors General (OIG) which remains unimplemented for one year or more from the annual budget justification submission date. The recommendations below apply specifically to this division of HHS. Please refer to the General Departmental Management budget justification for more information on the Department's overall progress in implementing GAO and OIG recommendations.

Appendix 1: OIG-GAO Open Recommendations

Report Number	Report Title	Report Date	Recommendation Text	Concur / Non-Concur	Implementation Timeline	Implementation Status	Implementation Updates and Constraints
GAO-16-13	National Institutes of Health: Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research	10/23/2015	To ensure effective implementation of the Inclusion Policy in a manner consistent with the Revitalization Act's provisions regarding the design of certain clinical trials, the NIH Director should examine approaches for aggregating more detailed enrollment data at the disease and condition level, and report on the status of this examination to key stakeholders and through its regular biennial report to Congress on the inclusion of women in research.	Concur	2019	Awaiting Disposition	
GAO-16-13	National Institutes of Health: Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research	10/23/2015	To ensure effective implementation of the Inclusion Policy in a manner consistent with the Revitalization Act's provisions regarding the design of certain clinical trials, the NIH Director should, on a regular basis, systematically collect and analyze summary data regarding awardees' plans to conduct analyses of potential sex differences, such as the proportion of trials being conducted that intend to analyze differences in outcomes for men and women.	Concur	2019	Awaiting Disposition	
GAO-16-13	National Institutes of Health: Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research	10/23/2015	To ensure effective implementation of the Inclusion Policy in a manner consistent with the Revitalization Act's provisions regarding the design of certain clinical trials, the NIH Director should report on this summary data and the results of this analysis in NIH's regular biennial report to Congress on the inclusion of women in research.	Concur	2019	Awaiting Disposition	

GAO-16-304	National Institutes of Health: Additional Data Would Enhance the Stewardship of Clinical Trials Across the Agency	3/10/2016	To enhance its stewardship of clinical trials across the ICs, the Secretary of HHS should direct the NIH OD to establish and implement a process for using those data.	Concur	2019	Awaiting Disposition	
GAO-16-573	Federal Research Grants: Opportunities Remain for Agencies to Streamline Administrative Requirements	7/22/2016	To reduce pre-award administrative workload and costs, particularly for applications that do not result in awards, the Secretary of Energy, the NASA Administrator, and the Secretary of Health and Human Services should conduct agency-wide reviews of possible actions, such as further use of preliminary proposals, to postpone pre-award requirements until after a preliminary decision about an applicant's likelihood of funding and, through OSTP's Research Business Models working group, coordinate and report on these efforts.	Concur	2020	In Progress	
GAO-16-573	Federal Research Grants: Opportunities Remain for Agencies to Streamline Administrative Requirements	7/22/2016	To better target requirements on areas of greatest risk, while maintaining accountability over grant funds, the Secretary of Health and Human Services, as part of the planned evaluation of the HHS regulation governing financial conflicts of interest in NIH-funded research, should evaluate options for targeting requirements on areas of greatest risk for researcher conflicts, including adjusting the threshold and types of financial interests that need to be disclosed and the timing of disclosures.	Concur	2020	In Progress	
GAO-16-573	Federal Research Grants: Opportunities Remain for Agencies to Streamline Administrative Requirements	7/22/2016	To further standardize administrative research requirements, the Secretary of Energy, the NASA Administrator, the Secretary of Health and Human Services, and the Director of NSF should coordinate through Office of Science and Technology Policy's (OSTP) Research Business Models working group to identify additional areas where they can standardize requirements and report on these efforts.	Concur	2020	In Progress	
GAO-16-616	NIH Biomedical Research: Agencies Involved in Indirect Cost Rate Setting Process Need to Improve Controls	9/28/2016	As NIH-DFAS begins formalizing its internal guidance, the Director of NIH-DFAS should develop detailed procedures for the completion and documentation of supervisory review of the indirect cost rate negotiation process to provide reasonable assurance that key control activities have been performed by the negotiator.	Concur	2019	Awaiting Disposition	Submitted documentation to GAO in December 2019 to close this recommendation as implemented.
GAO-16-616	NIH Biomedical Research: Agencies Involved in Indirect Cost Rate Setting Process Need to Improve Controls	9/28/2016	As NIH-DFAS begins formalizing its internal guidance, the Director of NIH-DFAS should establish a mechanism for tracking key milestones in the indirect cost rate-setting process, such as when indirect cost rate proposals are due.	Concur	2019	Awaiting Disposition	Submitted documentation to GAO in December 2019 to close this recommendation as implemented.
GAO-17-352	Youth With Autism: Federal Agencies Should Take Additional Action	5/4/2017	To implement the goals and policy priorities of the 2020 Federal Youth Transition Plan, the Federal Partners in Transition (FPT) workgroup--the	Concur	2020	In Progress	

	To Support Transition-Age Youth		Secretaries of HHS, Education, Department of Labor, and the Commissioner of the Social Security Administration--should develop a long-term implementation plan that includes milestones and specific agency roles and assignments.				
GAO-18-545	NIH Research: Actions Needed to Ensure Workforce Diversity Strategic Goals Are Achieved	8/10/2018	The NIH Director should develop quantitative metrics, evaluation details, and specific time frames to assess its current efforts to support investigators from underrepresented groups against its scientific workforce diversity strategic goals, and use the results of its assessment to guide any further actions.	Concur	2019	Awaiting Disposition	
A-04-16-04046	The National Institutes of Health Did Not Always Administer Superfund Appropriations During Fiscal Year 2015 In Accordance With Federal Requirements	2/16/2018	Issue new or updated guidance, as applicable, that provides clear examples to NIH grants management personnel of circumstances that require the review of Federal Cash Transaction Reports, corrective or enforcement actions against noncompliant grantees, and grant closeout procedures when grantees fail to provide final reports.	Concur	2020	In Progress	
A-04-16-04046	The National Institutes of Health Did Not Always Administer Superfund Appropriations During Fiscal Year 2015 In Accordance With Federal Requirements	2/16/2018	Formalize procedures for identifying and resolving negative unliquidated obligation balances recorded in NIH's accounting system.	Concur	2020	In Progress	

GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should develop department policies for managing hazardous biological agents in high-containment laboratories that contain specific requirements for training and inspections for all high-containment component agency laboratories and not just for their select-agent-registered laboratories; or direct the Director of CDC to provide these requirements in agency policies.	Concur	2020	In Progress	Guidance pulled from clearance for revisement to remove lab training section and embed in overall CDC training policy. Internal comments have been addressed in clearance process.
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should direct the Director of NIH and the Commissioner of FDA to require routine reporting of the results of agency laboratory inspections--and in the case of FDA, require routine reporting of select agent inspection results--to senior agency officials.	Concur	NA	In progress	FDA has a standing policy for managing hazardous biological agents in high-containment laboratories that includes reporting requirements (SMG 2130.8 and Directive 201710.2). In 2019, FDA began piloting a standardized Agency-wide laboratory safety inspection checklist to ensure that all laboratories are inspected rigorously and consistently. As part of the pilot, all laboratories are to be inspected during Q1-Q3 of the calendar year. Any corrective/preventative actions will be tracked and resolved locally during this inaugural

							year. The results of the inspections will be aggregated, and trends and significant findings will be reported to Agency senior leadership in Q4 of 2019. Beginning in 2019, OLS is committed to independently inspecting all high-containment and select agent laboratories and 1/3 of all other laboratories each year to ensure compliance with all laws, regulations, and consensus standards. (In other words, all laboratories will be inspected at least once every three years)
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should develop department policies for managing hazardous biological agents in high-containment laboratories that contain specific requirements for reporting laboratory incidents to senior department officials, including the types of incidents that should be reported, to whom, and when, or direct the Director of CDC and the Commissioner of FDA to incorporate these requirements into their respective policies.	Concur	NA	In progress	FDA has a standing policy for managing hazardous biological agents in high-containment laboratories that includes reporting requirements (SMG 2130.8, Directives 201710.2 and 2019.3). FDA also implemented a mechanism for incident reporting electronically to facilitate the investigation, resolution, and reporting of incidents. FDA continues to work with the Biosafety and Biosecurity Coordinating Council to establish a process for the routine reporting of the results of agency and select agent laboratory inspections to

							senior department officials.
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should require routine reporting of the results of agency and select agent laboratory inspections to senior department officials.	Concur	NA	In Progress	NIH has provided documentation to GAO as evidence they have implemented this recommendation.
GAO-16-305	High–Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety	4/19/2016	To ensure that federal departments and agencies have comprehensive and up-to-date policies and stronger oversight mechanisms in place for managing hazardous biological agents in high-containment laboratories and are fully addressing weaknesses identified after laboratory safety lapses, the Secretary of Health and Human Services should require routine reporting of incidents at CDC, FDA, and NIH laboratories to senior department officials.	Concur	NA	In progress	In August 2019, FDA reported that it continues to work with the Biosafety and Biosecurity Coordinating Council to establish a process for the routine reporting of these results but had not yet completed its actions.
GAO-16-642	High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk	9/21/2016	To increase scientific information on inactivation and viability testing, the Secretaries of Health and Human Services and Agriculture should coordinate research efforts and take actions to help close gaps in the science of inactivation and viability testing across high-containment laboratories.	Concur	2020	In Progress	The NIH and the CDC are actively working on revising the BMBL. The current plan is to incorporate a new appendix in the next revision that specifically addresses inactivation methods. This revision should take place in June 2020.
GAO-16-642	High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk	9/21/2016	To understand the extent to which incomplete inactivation occurs and whether incidents are being properly identified, analyzed, and addressed, the Secretary of Health and Human Services should direct the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) to develop clear definitions of inactivation for use within their respective guidance documents that are consistent across the Select Agent Program, NIH's oversight of	Concur	2020	In Progress	CDC program SMEs have completed agency review of the BMBL and are awaiting NIH concurrence of the revised document. Once this has been received, document will undergo CDC Clearance. The

			recombinant pathogens, and the Biosafety in Microbiological and Biomedical Laboratories manual.				electronic version will be released June 2020 and the printed version December 2020.
GAO-16-642	High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk	9/21/2016	To help ensure that inactivation protocols are scientifically sound and are effectively implemented, the Secretary of Health and Human Services should direct CDC and NIH to create comprehensive and consistent guidance for the development, validation, and implementation of inactivation protocols--to include the application of safeguards--across the Select Agent Program, NIH's oversight of recombinant pathogens, and the Biosafety in Microbiological and Biomedical Laboratories manual.	Concur	2020	In Progress	CDC program SMEs have completed agency review of the BMBL and are awaiting NIH concurrence of the revised document. Once this has been received, document will undergo CDC Clearance. The electronic version will be released June 2020 and the printed version December 2020.
GAO-16-642	High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk	9/21/2016	To help ensure that dangerous pathogens can be located in the event there is an incident involving incomplete inactivation, the Secretary of Health and Human Services should direct the Directors of CDC and NIH, when updating the Biosafety in Microbiological and Biomedical Laboratories manual, to include guidance on documenting the shipment of inactivated material.	Concur	2020	In Progress	CDC program SMEs have completed agency review of the BMBL and are awaiting NIH concurrence of the revised document. Once this has been received, document will undergo CDC Clearance. The electronic version will be released June 2020 and the printed version December 2020.

Appendix 2: OIG-GAO Closed, Unimplemented Recommendations

Report Number	Report Title	Report Date	Recommendation Number	Recommendation Text	Implementation Status	Reason for non-implementation
GAO-13-760	Biomedical Research: NIH Should Assess the Impact of Growth in Indirect Costs on Its Mission	10/31/2013	1	To help address the uncertainty NIH faces, related to the potential impact of increasing indirect costs on its funding of future research, the Director of NIH should assess the impact of growth in indirect costs on its research mission, including, as necessary, planning for how to deal with potential future increases in indirect costs that could limit the amount of funding available for total research, including the direct costs of research projects.	Closed, Unimplemented	Non-concur, recommendation is no longer valid

OEI-03-07-00700	How Grantee's Manage Financial Conflicts of Interest in Research Funded by the National Institutes of Health	11/18/2009	299-902-11-08-01505	NIH should develop and disseminate guidance on methods to verify researchers' financial interests.	Closed, Unimplemented	Non-concur, recommendation is no longer valid
OEI-03-09-00480	Institutional Conflicts of Interest at NIH Grantees	1/20/2011	299-902-12-08-01911	NIH should promulgate regulations that address institutional financial conflicts of interest.	Closed, Unimplemented	Requires legislative action
OEI-07-09-00300	NIH Administration of the Clinical and Translational Science Awards Program	12/20/2011	223-904-10-08-02495	NIH ensure that CTSA maintain official files in accordance with HHS policy. NIH must establish a single comprehensive filing system in which files are complete, current, easy to identify, easy to access, and separated by budget period. This would promote a coordinated approach to oversight for NIH staff and third-party reviewers	Closed, Unimplemented	Non-concur, recommendation is no longer valid
OEI-12-04-00310	HHS Agencies' Compliance with the National Practitioner Data Bank Malpractice Reporting Policy	10/11/2005	399-900-11-08-01148	NIH should implement a corrective action process that would address unreported cases.	Closed, Unimplemented	Requires legislative action
OEI-12-04-00310	HHS Agencies' Compliance with the National Practitioner Data Bank Malpractice Reporting Policy	10/11/2005	399-904-11-08-01149	NIH should improve internal controls involving case file management.	Closed, Unimplemented	Requires legislative action

TRANS-NIH INITIATIVES

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Trans-NIH Initiatives

Advisory Committee to the Director Working Groups

Institutes, Centers, and Offices (ICOs) Involved:
NIH-wide
Immediate Office of the Director (IMOD)
Office of Data Science Strategy (ODSS)

The Advisory Committee to the Director (ACD) brings together a diverse set of voices from outside NIH to provide consultation to the NIH Director on issues relevant to the NIH mission and goals for the conduct of biomedical research. The ACD meets twice yearly to make recommendations on program development, resource allocation, administrative regulations and policies, and other issues of interest to NIH. To make recommendations with the best information, the ACD forms working groups (WGs) and subcommittees to provide in-depth information and perspectives on specific topics.

Several currently active ACD WGs include the following:

- **Working Group on Diversity:** The group is a permanent WG of the ACD and has been charged with providing regular advice to the ACD and NIH Director on effective strategies to increase the representation of diverse individuals underrepresented nationally in biomedical research and to reduce disparities in research awards from diverse applicants underrepresented nationally in biomedical research. The goals of the WGD are to:
    - Enhance access and opportunities for all in order to foster a diverse scientific community
    - Enrich the educational, mentoring, and scientific experience of individuals in the biomedical research training pipeline
    - Promote personal and professional growth for biomedical researchers underrepresented nationally in biomedical research
    - Foster mutual respect and valuing of differences, as well as cross-cultural understanding and the realization of the value of diversity in science
    - Advance programs that prepare diverse individuals underrepresented nationally in biomedical research as scientific leaders.

  To accomplish these goals, the group promotes professional development of underrepresented researchers, programs which prepare underrepresented researchers to be scientific leaders, and identifies ways to enrich the education and training opportunities for diverse individuals.

- **Next Generation Researchers Initiative Working Group:** NIH has taken steps over the last several years to ensure the long-term success of biomedical research by supporting early and mid-career researchers. The Next Generation Researchers Initiative was designed to offer specific funding to these scientists. This WG, using a systems-oriented, data-driven approach to analyze the impact of this Initiative on NIH's scientific portfolio and workforce, advises NIH on related activities and provides mechanisms for collecting input on the Initiative from the research community. Their work has focused on considering independent assessments of productivity, advising on ways to support early-stage investigators, identifying overlapping

needs and initiatives across NIH especially as it relates to diversity, and assessing the effectiveness of such actions. The recommendations put forth in FY 2019 centered around a few main areas. First, they identified ways to modify the original NGRI policy, such as by defining a new class of "at risk" investigators who are at risk for losing all NIH support and leaving the scientific enterprise. They encouraged NIH to foster more collaboration and engagement with scientists across career stages to inform policy decisions. Strategies were also suggested to address salary support from NIH awards and improve career development for post-doctoral fellows. The WG also promoted sustainable training opportunities that incorporate diversity and inclusion, along with establishing policies requiring discrimination and harassment-free work environments. Finally, new metrics and access to data are needed to help continually understand the dynamics of the workforce, optimize workforce stability, as well as increase transparency in decision making at NIH. NIH staff are currently evaluating all of the recommendations, assessing which have the best opportunities for success, while also addressing any potentially unintended consequences.

- **Working Group on Artificial Intelligence (AI):** In 2019, the NIH Director announced the formation of an AI working group of the ACD. Coordinated by the OD, this ACD AI WG is identifying trans-NIH opportunities in AI and machine learning (ML), determining how NIH can best collaborate with computer and data science communities, defining approaches for NIH to encourage computer scientists to engage in biomedical research, and identifying the major ethical considerations related to AI in health research and care. Recommendations include a proposal to build large, diverse programs to foster development of a new field, BioMed ML and a call for new, large-scale datasets, built by multidisciplinary teams. Ethical principles for AI use are also a focus, including considerations for how datasets and algorithms can be labeled with data sheets and model sheets to help researchers use and reuse data and models appropriately, analogous to prescription medication labels that explain to patients how to safely use medications. The ACD AI WG reported their recommendations to the ACD in December 2019, and the ACD accepted the recommendations.[37] Over the coming months, NIH will work toward implementation. The recommendations are to:
    - Support flagship data generation efforts to propel progress by the scientific community
    - Develop and publish criteria for ML-friendly datasets
    - Design and apply “datasheets” and “model cards” for biomedical ML
    - Develop and publish consent and data access standards for biomedical ML
    - Publish ethical principles for the use of ML in biomedicine
    - Develop curricula to attract and train ML-BioMed experts
    - Expand the pilot for ML-focused trainees and fellows
    - Convene cross-disciplinary collaborators

- **HeLa Genome Data Access Working Group:** The HeLa Genome Data Access WG reviews research applications requesting access to HeLa cell line genomic sequence data. Formed in response to an agreement with the family of Henrietta Lacks (from whom the cells were derived), this WG respects the wishes of family members who hope to see the HeLa genomic

[37] https://acd.od.nih.gov/documents/presentations/12132019AI_Report.pdf

sequence data used for the advancement of biomedical research but want to ensure concerns surrounding the family's consent and privacy were addressed The WG, on which three members of the Lacks family currently serve, provides a review mechanism by which researchers can apply to NIH to access and use the data in a specific research study, and the WG reviews to ensure that specific terms of use are adhered to. This process, including the terms of use, was developed in consultation with the Lacks family and represents a novel and historic partnership between NIH and the family of Henrietta Lacks.

- **Working Group on Changing the Culture to End Sexual Harassment:** As a part of a large NIH-wide effort to end sexual harassment in biomedical research, the WG on Changing the Culture to End Sexual Harassment has assessed the current state of reporting, investigation, and remediation at NIH-funded organizations, proposed actions for the NIH to promote safe inclusive workplaces, and suggested systemic changes to mentored networks and leadership to change climate and prevent harassment. Additionally, the WG was charged with, among other things, developing strategies for encouraging research on anti-harassment policies, procedures, and training, including measures and evaluations of their effectiveness. This WG presented interim recommendations to the ACD in June 2019, including an interim recommendation to treat professional misconduct, including sexual harassment, as seriously as research misconduct. The WG presented its report and final recommendations to the ACD in December 2019. The key themes from the report accepted by the NIH Director include:
    - Increase transparency and accountability in reporting of professional misconduct, especially sexual harassment;
    - Establish mechanisms for restorative justice;
    - Ensure safe, diverse, and inclusive research and training environments; and
    - Create system-wide change to ensure safe, diverse, and inclusive research environments

- **Working Group on Enhancing Reproducibility and Rigor in Animal Research:** In response to growing concern about the rigor and replicability of animal research for improving health outcomes, this group has been charged with assessing and making recommendations to enhance the reproducibility and rigor of animal research by improving experimental design, optimizing translational validity, enhancing training, and increasing the transparency of research studies involving animal models. Building on the efforts already undertaken by NIH to improve rigor, reproducibility, and transparency, and taking into account work done by outside organizations, including the National Academies of Sciences, Engineering, and Medicine, the National Centre for the Replacement, Refinement, and Reduction of Animals in Research, and scientific societies (e.g., American Physiological Society, Society for Neuroscience), the WG will consider how training in animal research can be improved, assess the current state of science in alternative methods to animal models, how animal models of human disease are currently developed, and their use in translational research. This WG is expected to make its recommendations in late FY 2020.

Harnessing Artificial Intelligence for Health

ICOs Involved:
NIH-wide
Office of Data Science Strategy (ODSS)
Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI)
Immediate Office of the Director (IMOD)

The Potential of Artificial Intelligence for Health Research

Artificial Intelligence (AI) is not new, but advances in technology and data collection in the past decade have rapidly advanced AI, and it is now being integrated into every realm in human society. AI methodologies offer the ability to make sense of complex datasets that are too large for humans to manually process, to reduce noise in the data, and to find the most relevant data relating to the question being asked. AI has the potential to accelerate biomedical and clinical research, and improve clinical care, if used with an understanding of its limitations and consideration of the ethical complications. AI could be particularly beneficial in places with limited access to health care, for example, patients and populations in middle and low resource areas. Researchers use AI in research-related activities in efforts to move toward translation to use in the clinic; clinicians use AI to continuously learn and understand their patients; patients use AI to better understand themselves; society uses AI to enable computational creativity (i.e., to complement and enhance human intelligence, rather than replace it); policymakers regulate AI to ensure its ethical and safe use. Across the NIH, AI is being applied to various areas of health research in order to fully realize this potential.

The NIH Office of the Director (OD) hosted a workshop, Harnessing Artificial Intelligence and Machine Learning to Advance Biomedical Research, to centralize the NIH's interest in AI and gather feedback from experts in the community. Four major needs in AI were identified – preparing data for AI use, applying AI ethically, increasing engagement with computer science communities, and improving AI methods and interpretation at NIH. As discussed in the previous section on Advisory Committee to the Director Working Groups, in 2019, the NIH Director announced the formation of an AI WG of the ACD that made eight recommendations for how NIH can best collaborate with computer and data science communities, encourage computer scientists to engage in biomedical research, and identify the major ethical considerations related to AI in health research and care.

Leveraging Artificial Intelligence across the NIH

Application of AI to biomedical research is part of a larger effort at NIH to harness big data. Specifically, rapid advances in data generation, computing, networking, and algorithms, such as artificial intelligence, are intertwined in a newly evolving digital infrastructure. For example, with the rise of DNA sequencing and other technology advances, rapid and high throughput data generation drove the need for advances in information-based algorithms and memory-rich computers that made it possible to interpret these data in new ways. Today, biomedical data is measured in the petabytes and is comprised of data types ranging from DNA sequences to wearable activity sensor-generated outputs, like heartrate. This increase in pace, scale, and complexity of biomedical data, which can be used to understand and alleviate diseases, underpins the notion of 'big data' for biomedical research. These types of data are ripe for

analysis through the use of AI. NIH's Office of Data Science Strategy coordinates trans-NIH efforts to implement the NIH Strategic Plan for Data Science,[38] which aims to keep NIH at pace with rapid changes in biomedical data science, including seeking out new applications of AI to biomedical research.

NIH ICOs continue to pursue the application of AI approaches in their scientific domains. For example, the National Advisory Council on Aging recently approved in concept a Funding Opportunity Announcement (FOA) on Artificial Intelligence and Technology Centers for Aging Research. Each Center will facilitate the development of a pipeline of technologies representing themes such as early detection of cognitive and functional decline; protection against financial abuse and fraud; safe and comfortable aging in place; and effective management of multiple chronic conditions. NIH anticipates that these Centers will be active in FY 2021. The National Library of Medicine (NLM) has utilized AI to analyze medical images that can improve detection, diagnosis, and treatment of disease, resulting in advances such as: a screening tool for improving classification of cervical cancer and assisting in early treatment in low-resource areas; novel approaches to classify the severity of age-related macular degeneration (AMD) and predict risk of progression to late-stage AMD better than existing clinical standards; an algorithm to detect abnormalities in chest X-ray images and screen for tuberculosis in low-resource settings for populations with high incidence of HIV; and an algorithm that screens for malaria with 99 percent accuracy by detecting the presence of the malaria-causing parasite in red blood cell images. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) is supporting use of a machine learning (ML) framework to predict severe maternal morbidity. Severe maternal morbidity, or life-threatening pregnancy complications at delivery, has been increasing steadily, affecting more than 50,000 women in the United States in 2014. Researchers aim to analyze population-based data, linking Maryland state databases with hospital survey data, in order to develop techniques that can predict maternal risks early. Identifying key predictors of severe maternal morbidity can help ascertain health disparities, strengths and weaknesses in obstetric care, and prevent adverse maternal and neonatal outcomes. The National Heart, Lung, and Blood Institute (NHLBI) is building a cloud-based computing infrastructure under its BioData Catalyst hosting large volume of image data and tools supporting AI computing for image data. Its beta version with data on 20,000 chest CT scans from COPDGene is scheduled to be released in late FY 2020. The National Human Genome Research Institute (NHGRI) funds projects that utilize AI/ML in genomics with aims to improve our understanding of the regulatory code, annotate genome structure and function, and elucidate the effects of genetic variation on molecular and disease phenotypes. The ENCODE Data Analysis Center uses machine learning techniques to gain novel insights about the relationship between classes of functional elements, with the goal of annotating functional elements of the genome. The National Center for Advancing Translational Sciences (NCATS) Biomedical Data Translator program is tackling a major challenge in translation, connecting highly compartmentalized data—including health records, publications, chemical biology datasets—across diseases and disciplines. Translator is not only connecting data, but it is creating software that will lead to AI-guided knowledge mapping to help inform research

[38] NIH Strategic Plan for Data Science. https://datascience.nih.gov/strategicplan

directions. While primarily a research tool, and not intended for clinical decision support, Translator also has the potential to inform areas like undiagnosed diseases or ultra-rare diseases, where it is unlikely that clinicians have seen these types of cases. While such AI/ML algorithms can support clinical care decisions, national standards and protocols for validating such algorithms don't yet exist. The Clinical and Translational Science Awards (CTSA)-supported Center for Data to Health (CD2H) is developing best practices (i.e., Good Algorithm Practices) and aiming to establish standards for transparency, reproducibility, and understandability for use of such algorithms in clinical practice. Looking to FY 2021, the Common Fund is also exploring a potential program in AI based on the December 2019 recommendations of the ACD AI WG. Generating data that is amenable to AI, supporting research on the ethical use of AI approaches, and training a suitable workforce are likely themes for the program.

Lastly, NIH is harnessing the power of AI for use with internal NIH data to support data-driven decision-making. The Office of Portfolio Analysis (OPA) uses AI-based approaches to support analysis of the biomedical research landscape and inform data-driven decision-making by NIH leadership. In addition, the Office of Extramural Research (OER) is currently collaborating with the National Institute on Aging to determine if machine-learning techniques can enhance the current Research, Condition, and Disease Categorization (RCDC) process for identifying aging-related research activities. The National Institute of General Medical Sciences (NIGMS) has used natural language processing and machine learning for the grant referral process. Benefits include substantial time savings, allowing experts time to work on higher value tasks, additional objectivity, standardized results, and better accuracy. OER and NIGMS are collaborating to incorporate this algorithm into NIH-wide Enterprise Systems.

Continued Engagement with Artificial Intelligence

NIH ICOs are also hosting workshops to engage stakeholders and identify key priorities to continue to integrate AI into their portfolios. In October 2019, NHLBI organized a workshop on imaging genomics. AI and Machine Learning is one of the major topics discussed in the workshop. A white paper is in progress. The NIH Artificial Intelligence Interest Group, Office of Intramural Research, and NIH AI WG for Autonomous Therapeutics held a joint workshop in October 2019 to convene expertise on the potential of AI. A workshop funded by the National Institute of Environmental Health Sciences (NIEHS), "Leveraging Artificial Intelligence and Machine Learning to Advance Environmental Health Research and Decisions", hosted a range of scientists to present AI applications in environmental epidemiology, chemical hazard assessment, and fields beyond environmental health sciences. The workshop was held in Washington, DC in June 2019 and sponsored by the National Academies of Sciences, Engineering, and Medicine (NASEM). The National Institute of Biomedical Imaging and Bioengineering (NIBIB) has convened two workshops on the promise and challenges of AI technologies in medical imaging to provide a roadmap to optimize the use of AI in biomedical imaging. The first workshop held in August 2018 resulted in the issuance of The Roadmap for AI in Medical Imaging. A follow-up workshop in November 2019 focused on developing the partnerships necessary to realize the tremendous potential of AI use in medical imaging. Both workshops included participation by multiple ICs, academia, and radiological societies. These events are continuing to expand application of AI approaches to all areas of NIH-supported health research.

***All of Us* Research Program**

ICOs Involved:
NIH-wide
All of Us Research Program

Program Overview:
Thirty years after Congress funded the Human Genome Project (HGP)[39] the *All of Us* Research Program,[40] a key component of the Precision Medicine Initiative and the 21st Century Cures Act (P.L. 114-255), continues its progress toward enrolling at least one million or more participants who reflect the rich diversity of the United States. The program is an ambitious effort to accelerate health research, medical breakthroughs, and to develop individualized care. Precision medicine would not be possible without the HGP's pivotal step towards discovery in mapping the DNA sequence of the entire human genome. Building on the knowledge gained through the HGP, *All of Us* will have the scale and scope to enable research for a wide range of diseases, both common and rare, as well as increase our understanding of health and wellness. Additionally, a research program of this size will have the statistical power to detect associations between environmental and/or biological exposures and a wide variety of health outcomes.

All of Us is a participant-engaged, data-driven enterprise supporting research at the intersection of human biology, behavior, genetics, environment, data science, computation, and much more to produce new knowledge and develop more effective ways to treat and prevent disease. The program officially opened for enrollment in May 2018 and currently enrolls participants 18 years of age or older from all 50 states, D.C., and the five populated U.S. territories through a network of more than 290 enrollment sites. This network includes regional medical centers, Federal Qualified Health Organizations (FQHC), Veterans Affairs (VA) medical centers, and local laboratories as part of the direct volunteer pathway. The program collects a variety of biomedical information from participants, including questionnaires, electronic health records (EHRs), physical measurements, data from digital health technologies, and biospecimens. As of mid-December 2019, more than 305,000 people had consented to join the program as the first step in the participant journey, including more than 235,000 core participants who have completed all the initial steps of the protocol (consent, health record authorization, biospecimen donation, and survey data).

A total of 34 health care provider organizations have uploaded EHR data on more than 150,000 participants. The current recruitment rate is approximately 3,000 core participants per week.

Diversity is a key component of the *All of Us* Research Program because the program wants to ensure that all people benefit from the new biomedical advancements made with *All of Us* data. The program plans to achieve its diversity goals through partnerships with organizations that have ties to, and can assist with the long-term engagement of, participants from communities that have been historically underrepresented in biomedical research (UBR). *All of Us* considers the following populations historically underrepresented: racial and ethnic minority groups; children and seniors; sexual and gender minorities; people with disabilities; people with barriers

[39] www.genome.gov/human-genome-project
[40] www.allofus.nih.gov/

in access to care, have low economic status, or have low educational attainment; and rural residents. Of the core participants as of mid-December 2019, more than 50 percent self-identify as members of racial and ethnic minority groups and 80 percent meet the program's definition of UBR; these percentages exceed the program's original goals of 50 percent and 75 percent, respectively.

True to one of the program's core values, the program considers participants to be its partners. *All of Us* participants are integrated into the program's governance in numerous ways by serving on boards, committees, and task forces, alongside researchers and staff at the local and national levels. Participant partners in *All of Us* provide feedback on multiple elements of the program, including program design, policies, and specific participant-facing elements. Participants will also be able to identify their preferences for what information they would like returned to them. The participant relationship is supported by engagement efforts that establish and maintain the trust needed for participants to join and remain in the program.

As another key element of the *All of Us* engagement strategy, the program has established a diverse network of approximately 40 funded community partner organizations and many more unfunded grassroots community partners across the country. These entities support engagement, outreach, and dissemination of *All of Us* information to diverse communities and populations, including African Americans, Asians, Latinos/Hispanics, older and rural adults, and sexual and gender minorities. The program also has an ongoing partnership with the National Network of Libraries of Medicine (NNLM), which further extends program outreach across the country. Establishing authentic engagement with participants and providing value are key to continued recruitment and long-term retention of participants.

Scientific and Programmatic Roadmap:

All of Us continues to take advantage of innovative technological and scientific opportunities to guide amendments to the program's evolving protocol and examine the quality and utility of the data the program is collecting. The program anticipates that the data collected will help to identify risk factors and biomarkers (including biological and genetic factors, environmental exposures, lifestyle choices, habits, and social determinants) to improve health by bringing about more efficient and accurate diagnosis and screening, leading to a better understanding of disease in diverse populations, more targeted use of existing therapeutics, and the development of new treatments. In the future, the program plans to develop further iterations of its protocol, which may include additional biospecimen collection and inclusion of other new data elements. In these efforts, *All of Us* will continue to engage with NIH personnel, research communities, participants, and other stakeholders to gather their input on the best ways to shape the future data collection and scientific efforts of the program.

In August 2019, *All of Us* leadership published an article in the *New England Journal of Medicine* describing the program and its progress to date.[41] It details *All of Us*' unique aspects such as a focus on diversity, the nationwide scale and accessibility, and the return of data to participants. The value of the program resides in the richness of data being collected, which will provide researchers the ability to analyze intersections among biological, environmental, and behavioral influences. The program is also leveraging EHR data to provide researchers valuable

[41] www.nejm.org/doi/full/10.1056/NEJMsr1809937

historical health data and piloting a direct volunteer pathway model that leverages new tools and resources to optimize the participant journey – simplifying the process for interested individuals living anywhere in the United States to join and remain enthusiastic partners. While the techniques to collect EHR data through the direct volunteer enrollment pathway are in their infancy, these revolutionary approaches may transform how medical research is collected and utilized by researchers in the future.

Trans-NIH Collaboration:
All of Us is building a research resource that may be utilized across the NIH and the entire biomedical research enterprise. The program hosts a trans-NIH committee whose members act as liaisons between the program and the NIH ICOs. This committee serves as a critical connection to the ICOs' strategic goals and provides input on the scientific design of *All of Us*. This includes the variables to be collected on all participants, opportunities to identify scientific partnerships and ancillary studies that may collect data within or in addition to the *All of Us* data collection protocol, and the tools and support needed for funded researchers to use the platform to ask key precision medicine questions. Additionally, the *All of Us* Director formed an Institute and Center (IC) leadership group of 13 IC Directors that provides strategic input and advice about the future of the program. Along with these trans-NIH committees, *All of Us* currently maintains a partnership with the NNLM, focusing on consumer access of high-quality health information to UBR communities throughout the United States, while raising awareness of precision medicine and the importance of the program. *All of Us* is currently in the process of establishing additional partnerships across NIH, including with the National Institute of Mental Health to incorporate online modules that will capture cognitive and behavioral data from program participants and with the NICHD using PregSource[42] to capture information on pregnancy for participants that are or become pregnant.

Future trans-NIH collaborations that are in the early planning stages include partnerships with NHLBI to evaluate the burden of sickle cell trait across the population; NHGRI to collaborate on the responsible return of genetic information and on ethical, legal, and social implications research; the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) on precision nutrition; and the National Institute on Drug Abuse (NIDA) to develop a mechanism to link data of future *All of Us* participants dually enrolled in the Longitudinal Study of Adolescent Brain Cognitive Development (the ABCD Study). *All of Us* will continue its efforts to engage NIH ICs to leverage resources to answer a wide range of biomedical research questions and assist with targeted outreach to the research community.

Investment in the Future:
The *All of Us* Research Program will continue to make progress towards reaching its long-term target goal of recruitment and retention of one million or more people from diverse populations and walks of life. The program plans to achieve these goals by establishing an authentic, bi-directional, engagement experience and by working with participants and community partners to create and leverage new and innovative tools and resources to optimize the participant journey, making it as easy as possible for interested individuals living anywhere in the United States to join. The program also continues to refine and streamline the enrollment experience through piloting a self-guided participant journey, which flows as a series of steps rather than all at once,

[42] pregsource.nih.gov

that is scalable and allows for individuals who are not located near traditional research institutions to participate in the program. Additionally, the program also plans to support targeted regional campaigns aimed at increasing UBR enrollment.

Along with enrolling new participants, retaining current participants is a top priority for the program. The program plans to achieve these goals through enhancements to its digital and in-person participant experience, the responsible return of genetic and health information to participants, and the establishment of long-term relationships with participants who are true partners.

All of Us will eventually deliver the largest, richest biomedical dataset of its kind that is easy to use and accessible to the research community. Although most research programs similar to *All of Us* grant researchers access to data on a project-by-project basis, *All of Us* has developed a "passport model" through which researchers will be approved for broad data access to study any topic that meets the program's criterion for allowable use. In May 2019, the program launched its interactive Data Browser[43] to provide the public a first look at aggregate participant data. This tool allows researchers to begin to generate hypotheses and assess the potential of *All of Us* data for their studies. The program plans to open additional data to researchers through the beta release of the Researcher Workbench in 2020. *All of Us* will be a national resource that will grow richer over time as more participants join; the program adds new data types, from digital health data to whole genome sequences; and participants continue their involvement over many years.

Recent *All of Us* awards have laid the foundation for the future return of individual genetic results responsibly to participants who wish to receive them. With the funding provided by Congress, *All of Us* funded three premier genome centers[44] and established a nationwide genetic counseling resource[45] that will enable the responsible return of genetic results to participants. *All of Us* anticipates beginning to return individual genetic results to participants in 2020. *All of Us* entered into a partnership with the NCATS to fund a fourth genome center to test advanced sequencing tools and explore more elusive parts of the genome. Through this additional NCATS funding, *All of Us* will be able to offer approved researchers an even greater depth of genetic information than originally planned, making the resource even more valuable for them and the diverse communities we seek to serve.

All of Us is continually expanding methods of enrolling participants "where they are," including initiating a pilot program that allows participants to send in a saliva sample via the mail. The program also supports two mobile units that travel across the country to educate potential participants about the importance of precision medicine and support on-site account registration; one unit is also equipped for participants to provide physical measurements and biosamples onboard.

[43] www.researchallofus.org
[44] www.allofus.nih.gov/news-events-and-media/announcements/nih-funded-genome-centers-accelerate-precision-medicine-discoveries
[45] www.allofus.nih.gov/news-events-and-media/announcements/all-us-research-program-issues-funding-opportunity-genetic-counseling-resource

The enrollment of children in the *All of Us* Research Program has been and remains a priority. The program is building a team to lead the complex efforts necessary for the future enrollment of children. In order to do this responsibly there are important considerations including ensuring compliance with state legal requirements, having the appropriate consent and assent procedures required for children to join the study, enabling variable data collection methods across the childhood lifespan, considering the challenges of returning information, and managing different communications and informational needs for child participants and their guardians at each developmental stage. The program is cognizant of the need to maximize the long-term scientific utility of the pediatric data collected, ensuring that data from the pediatric protocol has the power to advance precision medicine research for participants who continue in the program as adults. *All of Us* understands the urgency and critical importance of enrolling this population into the cohort and acknowledges the excitement from the pediatric research community. The program's careful approach will enable a wide range of important precision medicine discoveries to improve children's health while also being mindful of the sensitivities and protections required to include minors.

Through the scale, scope, and accessibility of its data, *All of Us* will be positioned to address scientific questions from across the biomedical research enterprise and be leveraged by the NIH as a whole. For example, the program's data will be able to answer questions such as:

- Can a risk profile that includes genetic and other factors better explain and predict type 2 diabetes?
- Can we develop and validate machine learning approaches to diagnosing various cancers at earlier stages?
- How do non-pharmacological interventions impact health/resilience?
- What are the genetic factors associated with maternal mortality in African American women?
- What are the factors that influence vulnerability and resilience for opioid misuse in the face of chronic pain?

Ultimately, the program aims to enable research that will increase wellness and resilience, and promote healthy living; reduce health disparities and improve health equity; develop improved risk assessment and prevention strategies to preempt disease; provide earlier and more accurate diagnosis to decrease illness burden; and improve health outcomes and reduce disease burden through improved treatment and development of precision interventions. The program's approaches to meet participants where they are, engage them as true partners, and provide broad data access will transform how medical research is conducted in the future.

The Brain Research through Advancing Neurotechnologies (BRAIN) Initiative

ICOs Involved:
National Eye Institute
National Institute on Aging
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institute on Deafness and Other Communication Disorders
National Institute of Mental Health
National Institute on Minority Health and Health Disparities
National Institute of Neurological Disorders and Stroke
National Center for Complementary and Integrative Health
National Institute on Drug Abuse
National Institute on Alcohol Abuse and Alcoholism
National Institute of Biomedical Imaging and Bioengineering

Program Overview:
Dysfunction of brain circuits underlies all the neurological, psychiatric, sensory, and substance use disorders. Until recently, research tools have not been powerful enough to answer fundamental questions about how brain circuits work, and what goes wrong in these diseases: How many cell types make up the 170 billion cells in the brain? How are these cells connected to one another? How does the flow of information through the circuits of interconnected cells in the brain enable us to move, sense, think, communicate, and make us who we are as individuals? The BRAIN Initiative takes advantage of emerging opportunities, arising from decades of investment across many areas of science and engineering, to develop and apply technologies to answer these profound questions. Solutions for those suffering with neuro/mental/substance abuse disorders will come from seeing how malfunctions of brain circuits drive the many brain disorders.

Since NIH launched the BRAIN Initiative in 2014, Congress has expressed continuing interest and support through the 21st Century Cures Act, in yearly Appropriations report language, at hearings, in visits to the NIH, and during many other discussions with the NIH leadership.

From the Initiative's inception, the report BRAIN 2025: A Scientific Vision[46] has provided an overarching vision, operating principles, concrete goals, and milestones for this many faceted program. A stellar group of independent, interdisciplinary scientists, under the aegis of the NIH Advisory Committee to the Director, developed the BRAIN 2025 plan through extensive interactions with the scientific community. The Initiative builds on progress in neuroscience, optics, genetics, physics, engineering, informatics, nanoscience, chemistry, mathematics, and other disciplines to underpin a research program of unprecedented scope.

As befits the breadth of the program, the Initiative is highly collaborative within NIH, across Federal agencies, and with private organizations and the international scientific community. Scientific and engineering staff from 10 NIH Institutes and Centers manage the program through fully integrated teams. A Multi-Council Working Group (MCWG), with members from

[46] https://www.braininitiative.nih.gov/strategic-planning/brain-2025-report

participating Institute and Center Advisory Councils, provides advice and oversight through 10 Institute and Center Advisory Councils. Representatives from the Food and Drug Administration (FDA), National Science Foundation (NSF), Defense Advanced Research Projects Agency (DARPA), and Intelligence Advanced Research Projects Activity (IARPA) bring their expertise and coordinate activities through the MCWG. Together with non-profit and academic members of the BRAIN Initiative Alliance, the Initiative has engaged talent from academia and companies across a broad spectrum of science and engineering throughout the United States.

The seven priorities of the BRAIN 2025 plan, each with detailed goals and milestones, guide the activities of the BRAIN Initiative. These priorities are:

Discovering diversity: Identifying all the diverse brain cell types is essential to understand how brain circuits work and to develop research tools and therapies that precisely target specific cell types. The nearly 170 billion cells in a human brain differ in location, shape, connections, activity, and in their molecular composition, presenting a formidable challenge.

Maps at multiple scales: To understand how brain circuits work and solve the vexing problems of brain disorders, researchers must map the brain's anatomical and functional connections at multiple scales, from the major nerve fiber "highways" connecting areas of the brain to the trillions of microscopic synapses that connect individual cells.

The brain in action: To observe brain circuits in action, researchers must develop and apply tools to monitor simultaneously the activity of the thousands of brain cells, in real time, with millisecond time resolution, as they carry out their functions.

Demonstrate causality: By altering the activity of specific nerve cells in a brain circuit as an animal behaves, researchers can move beyond observation to demonstrating how circuits cause behaviors. Just as understanding how faulty genes cause disease has led to therapies for gene disorders, understanding how circuit malfunction underlies brain disease points the way toward reestablishing healthy circuits.

Theory and data analysis tools: Projects that monitor activity of thousands of nerve cells, map millions of synaptic connections, or assess activity of all genes in the myriad cell types of the brain generate immense amounts of data, which presents extraordinary opportunities and challenges. The data is of many types and scales—anatomical data from whole brain imaging to high resolution electron microscopy, physiological data from many individual cells to whole brain regions, and molecular data on genes and proteins, among others. Theories, simplifying principles, and testable models are essential to understand what this data tells us about how the brain works, what goes wrong in disease, and to predict the effects of altering brain circuits.

Advancing human neuroscience: Developing technologies to understand the human brain and treat its disorders presents special challenges, because of the human brain's size, complexity, and sensitivity to intervention, and the ethical caution that must guide research on the organ that is at the core of what makes us human.

From BRAIN Initiative to the brain: Integrating the new technological and conceptual approaches, which range from the nanoscale to whole organism behavior, is essential to discover how dynamic patterns of brain activity are transformed into cognition, emotion, perception, and action in health and disease. This integration is the ultimate goal of the BRAIN Initiative.

Scientific Highlights:
The BRAIN 2025 report advised NIH to monitor progress, adapt to the rapidly changing scientific and technical landscape, and take advantage of new opportunities arising from the Initiative itself and other areas of science and engineering. Following that recommendation, the ACD formed a new external scientific working group, the ACD BRAIN Initiative WG 2.0, to assess progress and identify how the Initiative can best invest to realize its vision. After intensive investigation and outreach to the research community, the group reported to the ACD in June 2019 that the BRAIN Initiative is making significant progress on all seven major priorities of the plan, with many specific objectives and milestones already accomplished, and unanticipated progress in some areas. The ACD also engaged a separate working group, which also reported in June 2019, to ensure that the BRAIN Initiative continues to consider the ethical implications of its pioneering studies on the workings of the brain and how these will be understood and applied.

Cell diversity is one priority on which progress has been remarkable, well ahead of what was anticipated. This enabled the multi-site BRAIN Initiative Cell Census Network to scale up using high throughput methods and begin developing a comprehensive mouse brain cell atlas and to advance cell type identification into human brains. Several powerful brain mapping and activity monitoring tools that were in their infancy when the BRAIN Initiative began have also dramatically improved. Researchers throughout neuroscience are rapidly adopting these advances, which range from better anatomical and functional brain imaging, to genetic "barcodes" for mapping connections, and automated 3D reconstruction from highly magnified electron microscopy of serial brain sections. Optical monitoring methods now enable researchers to simultaneously monitor the activity of thousands of brain cells, capturing the contributions of every nerve cell in simple experimental animals as the animals carry out simple behaviors. Likewise, the BRAIN Initiative is both dramatically enhancing existing methods and developing entirely new technologies to manipulate circuits. These methods variously use electromagnetic, ultrasound, chemical, and optical techniques in laboratory animals, and may be adaptable to treat human patients in the future.

To make useful data available to the research community, the BRAIN Initiative, using the authorities in the 21st Century Cures Act, has issued a strong data sharing policy. The Initiative has also supported the development of data standards, developed data archives for the various types of data, and is developing and disseminating data analysis tools.

From its inception, the focus of the BRAIN Initiative has been on understanding the normal brain, largely in laboratory animals. This will, in due course, provide the tools and knowledge to combat human brain diseases that have proven so challenging to medical science. The extent to which advances within the Initiative itself and the use of these new capabilities throughout neuroscience programs are already stimulating new opportunities against human disease is encouraging. The progress in developing high throughput methods to study cell diversity in

laboratory animals is now enabling researchers for the first time to determine precisely which human brain cells are affected by diseases such as Alzheimer's, autism, and Zika virus infection, with the potential to direct treatment to those cells. Cell typing has also provided insights about why so many drugs that are effective in mouse models of brain diseases do not translate to humans. New methods to release circulating drugs from carriers using ultrasound have demonstrated proof in principle of a strategy to deliver active drugs precisely where they are needed in the brain. "Closed-loop" deep brain stimulation (DBS), which monitors brain activity and automatically adjusts stimulation accordingly, has shown promise for treating Parkinson's disease, and DBS is being explored for depression, epilepsy, and several other disorders. Noteworthy brain computer interface projects have, for example, decoded speech directly from brain activity and developed a feasible approach to restore vision using a visual neural prosthesis. The BRAIN Initiative has also targeted initiatives to bring new neurotechnologies to bear on developing new approaches to addiction and to non-addictive treatments for pain to address the opioid crisis. Just as the Human Genome Project had an impact far beyond medicine, the BRAIN Initiative is also inspiring private sector developments, with major private sector investments based on neuroscience progress underway in artificial intelligence, computer hardware, and human computer interface systems.

Next Steps:
The BRAIN 2.0 WG recommended that the NIH BRAIN Initiative stay on the productive path that is underway; that is, continuing the development of technology while increasing the emphasis on application of the new methods to understanding brain circuits, as per the original plan. The WG also suggested many "tune ups" to specific goals and new milestones, now that many objectives of the original plan have been met or exceeded.

Among the general recommendations, the group also recommended increasing attention to organization of science as the Initiative moves forward. To capitalize on the value of data from the Initiative to neuroscience, BRAIN data should be FAIR (findable, accessible, interoperable, and reusable). To accomplish this, NIH must follow through on the data sharing policy that the Initiative issued in 2019 and on development of data standardization, archiving, and analysis tools that has begun. BRAIN must also renew the focus on human capital, which has been critical to progress since the Initiative's inception. Not only is there is a continuing need to engage scientists and engineers from a broad range of fields and background, but, as the Initiative progresses, translational and clinical scientists, and experts in quantitative domains become all the more essential. Throughout its programs, the Initiative must balance individual-investigator research with team science as new opportunities emerge.

None of the above cited recommendations from the BRAIN 2.0 group represent a notable departure from the original vision of the BRAIN 2025 report. However, the group did suggest that the BRAIN Initiative, given the remarkable progress to date, could now consider investing in larger scale, transformative projects that might propel neuroscience far into the future. These include opportunities from across all BRAIN Initiative priority areas, for example, a large scale project to generate methods to precisely access, manipulate, and model hundreds of clinically relevant brain cell types, a comprehensive cell-type atlas of the human brain, complete "connectome" maps of the mouse brain, or developing a truly specific circuit intervention for a

major human psychiatric or neurological disease symptom. The BRAIN Initiative is considering the feasibility and impact of these large-scale scientific opportunities for its next five years.

INvestigating Co-occurring conditions across the Lifespan to Understand Down syndromE (INCLUDE) Project

ICOs Involved:
National Cancer Institute
National Eye Institute
National Heart, Lung, and Blood Institute
National Human Genome Research Institute
National Institute on Aging
National Institute of Allergy and Infectious Diseases
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institute of Arthritis, Musculoskeletal and Skin Diseases
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Environmental Health Sciences
National Institute of Mental Health
National Institute on Minority Health and Health Disparities
National Institute of Neurological Disorders and Stroke
National Institute of Nursing Research
National Center for Advancing Translational Sciences
National Center for Complementary and Integrative Health
Office of the Director: Office of Research Infrastructure Programs, Office of Strategic Coordination (Common Fund), Immediate Office of the Director

In the last 25 years, the expected lifespan for people with Down syndrome (DS) has doubled, leading to a pressing need to understand the medical needs and challenges faced by individuals with Down syndrome as they age. The INCLUDE Initiative, a trans-NIH effort, is engaging diverse expertise across the agency to address the complex nature of Down syndrome and the need for a comprehensive approach. This effort is attracting new investigators into the field and is continuing to grow and support Down syndrome research with new opportunities across the spectrum of basic and clinical research, building a cohort of individuals with Down syndrome across the lifespan and developing outcome measures for impactful clinical trials tailored to these individuals. INCLUDE is hosting workshops to bring together patients and patient advocates, investigators, clinicians, and NIH staff to better engage the community and garner input on these research objectives.

Past: Launch of the INCLUDE Initiative
Beginning in FY 2018, the existing NIH Down Syndrome WG expanded to the 21 ICOs listed above, adding expertise to inform the development of the INCLUDE initiative. This broad representation across NIH captures the trans-NIH effort and appropriately reflects the complex nature of Down syndrome and the need for full engagement of NIH's collective scientific expertise. A research plan for the INCLUDE initiative was developed through the NIH Down Syndrome WG and posted on the NIH website to inform the Down syndrome community about its priorities and encourage the scientific community to apply for research funding.[47]

[47] www.nih.gov/include-project/include-project-research-plan

The INCLUDE effort is centered on the need for scientific discoveries aimed at improving the health of individuals with Down syndrome as well as the health of those without Down syndrome who share common co-occurring conditions including Alzheimer's disease, cancer, cardiovascular disease, immune system dysregulation, and autism, among others. This research opportunity has a unique "double benefit" in that chromosome 21 provides a genetic foothold and a starting point for a molecular understanding of these co-occurring conditions. Therefore, it has the potential not only to improve the health of those with Down syndrome, but also that of many others through a greater understanding of common conditions present, or absent, in individuals with Down syndrome.

The three primary components of the INCLUDE initiative are:

Component 1: Conduct targeted, high-risk, high-reward basic science studies on chromosome 21.

Component 2: Assemble a study population of individuals with Down syndrome.

Component 3: Include individuals with Down syndrome in existing and future clinical trials.

In the first year of INCLUDE, NIH supported 49 administrative supplements to existing grants, either to expand existing efforts on Down syndrome, or add a Down syndrome-related component to other grants. Thirteen ICs participated, and all three major components of the INCLUDE initiative were addressed, covering the waterfront of INCLUDE's research plan. The goal of these FY 2018 investments were to lay the critical groundwork needed for building this initiative and to further engage with the Down syndrome community and other stakeholders, informing further development of INCLUDE. Strategic use of administrative supplements in this first year also drew investigators into the field, leveraging ongoing work across the participating ICs and enabling individuals with Down syndrome to be pulled into existing cohorts and clinical trials quickly, a major concern in the DS community. The first scientific meeting of the INCLUDE project took place in November 2018 at NIH and gathered together clinical researchers to discuss optimal ways of conducting clinical trials in adults with Down syndrome who are at high risk to develop Alzheimer's disease, a major health challenge for adults with Down syndrome and their families.

Building INCLUDE into a full-fledged Trans-NIH Program

In FY 2019, this program continued to grow, shifting support towards new awards and Request for Applications (RFAs) developed following community engagement. Five FY 2019 Funding Opportunities covered a broad range of research areas related to Down syndrome, from basic to clinical research and focusing on transformative opportunities, preparation and initiation of clinical trials, and building the pipeline of Down syndrome researchers. Through these funding opportunities, 43 awards were made including support for four early-stage or new investigators and five training grants, expanding the pipeline of investigators in Down syndrome research.

Into the future of INCLUDE: An integral part of the NIH Down syndrome research agenda

Looking to FY 2020 and beyond, INCLUDE has released 12 FOAs (detailed below) in FY 2020 to further expand the INCLUDE Project. These funding opportunities will continue to invest in the three components of INCLUDE, with additional emphasis on component 2 (assembling a

study population of individuals with Down syndrome) following input from a scientific workshop "Planning a Virtual Down Syndrome Cohort Across the Lifespan," on September 23-24, 2019, which provided input on how to create a large cohort for natural history and biomarker studies -- to include current, smaller cohorts -- all critical aspects of the cohort development component 2 of the INCLUDE research plan.

The three RFAs developed in FY 2019 were re-issued in FY 2020 to further capitalize on those efforts, specifically continuing the R01 Transformative Research Award, the R21 Clinical Trial Readiness Research Award and the R61/R33 Phased Awards for Clinical Trials for Co-Occurring Conditions in Individuals with Down syndrome.

Two new RFAs were developed in FY 2020 that further address component 2. One solicitation will support the development of a center to coordinate the collection, storage, quality control, and harmonization of data and biospecimens related to the creation of a large clinical cohort of individuals with DS across the lifespan. This center will also provide an integrated data portal for investigators. The goal is to advance the diagnosis, management, and treatment of Down syndrome and its co-occurring conditions through the collection of pan-'omics datasets from existing and prospective DS clinical cohorts. A second opportunity will encourage applicants that propose to conduct primary data analysis or interpretation of DS data from existing cohorts or secondary analysis of publicly available NIH-funded datasets to enhance an understanding of DS across the lifespan. Expanded use of existing datasets and biorepositories will allow researchers to address research questions within the scientific scope of the INCLUDE project at relatively low cost and effort and enhance the value of INCLUDE investments in research.

In addition, three Notices of Special Interest released in FY 2020 specifically target fellowship and career development awards to continue to build the pipeline of Down syndrome researchers. Another new Notice of Special Interest aims at developing research models of Down syndrome to provide novel tools for understanding Down syndrome and assessing potential interventions. The remaining funding opportunities are Notices of Special Interest for administrative supplements and competitive revisions to continue to leverage ongoing work across NIH where needed, and new grants applications (R01) focused on Down syndrome across a range of scientific approaches.

Through this constellation of funding opportunities, all three components of INCLUDE continue to be further developed, with establishment of the data coordinating center a major step in development of a Down syndrome cohort. Two additional workshops are planned for Spring and Fall 2020 to address the state of the science for clinical trials in Down syndrome, and promising areas in basic research, respectively. NICHD will provide additional impetus for clinical trial development through INCLUDE by working with its national Pediatric Trials Network to incorporate cohorts of people with Down syndrome into their pediatric drug testing trials. In addition, NICHD will create a training program for these clinical researchers, using the expertise of currently funded researchers who study Down syndrome, on how to work best with individuals and families of people with Down syndrome in conducting clinical trials. This program could be applicable to including individuals with other intellectual and developmental disabilities in clinical research.

Lastly, NIH is revisiting its research plan on Down syndrome, last updated in 2014.[48] This plan will include an update on the INCLUDE research plan released in FY 2018 at the launch of the program. NIH will begin this strategic planning exercise by utilizing Requests for Information to garner input from the Down syndrome community, including the public-private Down Syndrome Consortium led by the NIH. This effort will provide a critical opportunity to re-assess program priorities as INCLUDE continues to mature as it enters its third year and will ensure continued strategic alignment between INCLUDE and the overarching goals of Down syndrome research across the NIH.

[48]www.nichd.nih.gov/sites/default/files/publications/pubs/Documents/DSResearchPlan_2014.pdf

NIH Pediatric Research Consortium (N-PeRC)

ICOs Involved:
NIH-wide
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Funding for pediatric research across NIH has increased steadily since 2013, reaching $4.5 billion in FY 2018. Nearly all of the NIH ICOs support some pediatric research. The NIH Pediatric Research Consortium (N-PeRC) is a trans-NIH initiative established in June 2018 to provide a venue for NIH ICs to harmonize activities related to pediatric research, explore gaps in the overall NIH portfolio, and share best practices to advance science across ICs. Initial efforts concentrated on surveying the global landscape of pediatric research and training at NIH to identify and articulate areas in which N-PeRC can work collaboratively to fill gaps or augment ongoing initiatives.

Making pediatric data resources more accessible – Currently, there are many pediatric datasets available to researchers but there is no central location that lists these resources and provides information on how to access them. One of N-PeRC's initial endeavors is to identify databases supported by NIH to explore development of a central location to list and link these databases. This would provide a single reference point for pediatric researchers to identify data that may be available for hypothesis testing and secondary analyses.

Expanding the pediatric research workforce – Pediatric training and career development efforts are currently supported by multiple NIH ICs, and N-PeRC members are discussing ways to coordinate and communicate these efforts to the child health research community. An initial analysis showed that support for pediatric training is broadly distributed across NIH ICs, just as support for pediatric research itself is broadly distributed across ICs.

Supporting pediatric reviewers – Development and maturation of the brain and other organs, ongoing changes in physiology and growth, and specific processes such as puberty are important considerations for research on diseases and conditions that affect children. N-PeRC has added representation from the Center for Scientific Review to help facilitate appropriate review, including identifying potential pediatric experts to serve on review panels for grant applications that require pediatric expertise.

Transition from pediatric to adult healthcare – Although many typically developing adolescents may find it challenging to transition to adulthood, individuals with chronic conditions (such as congenital heart disease) or intellectual or physical disabilities face increased challenges during the transition from pediatric to adult healthcare. Ensuring continuity of care for these individuals is vital for their health and wellbeing. N-PeRC members formed a working group to examine NIH's investment in this area and are now generating ideas for collaborative activities to begin to address gap areas.

Prioritize drug and device testing for pediatric labeling through the Best Pharmaceuticals in Children Act (BPCA) and other activities – Each of the ICs was asked to provide a list of the highest priority drugs relevant to each IC's focus on organ or disease. These suggestions will be

discussed and then considered for incorporation into the BPCA priority list.[49] N-PeRC is also reviewing NIH's research on pediatric devices to identify opportunities to work together across the agency.

In the future, N-PeRC will catalyze greater trans-NIH collaborations across pediatric research, especially in areas of common interest such as the transition of adolescent to adult healthcare and pediatric drug and device development. Expert meetings or workshops to assess the state of the science and/or gather input from external stakeholders could inform future efforts, including NIH funding opportunities and notices. N-PeRC will further analyze the available opportunities for training the next generation of pediatric researchers. N-PeRC anticipates a series of efforts to inform the pediatric community about little-known or overlooked training and career development opportunities in pediatric research. N-PeRC leadership will maintain strong links and regular communication with the domestic and global pediatric research communities to harmonize study designs if possible and to increase general awareness of funding opportunities and the availability of publicly shared resources such as the NICHD's Data and Specimen Hub. Finally, N-PeRC plans to promote further engagement with other federal partners that have substantial investments in child health.

[49] www.nichd.nih.gov/sites/default/files/inline-files/2018PriorityList-Feb19.pdf

NIH Helping to End Addiction Long-term (HEAL) Initiative

ICOs Involved:
National Heart, Lung, and Blood Institute
National Institute of Allergy and Infectious Diseases
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institute of Arthritis, Musculoskeletal and Skin Diseases
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
National Center for Complementary and Integrative Health
National Institute on Drug Abuse
National Center for Advancing Translation Sciences
National Institute for Biomedical Imaging and Bioengineering

Program Overview:
The national crisis of opioid misuse, addiction, and overdose, one of the largest and most complex public health crises that our nation has faced, continues to affect communities across America. The crisis has many contributors, including the need for pain management among the 100 million Americans with chronic pain at risk for opioid misuse, the limited number of effective options for the prevention and treatment of opioid use disorder, and the failure to implement the successful interventions that we have.

To advance scientific breakthroughs aimed at tackling the crisis, the HEAL Initiative, a major coordinated effort through the NIH Office of the Director, was launched in April 2018. This trans-NIH effort builds on well-established NIH research to accelerate scientific solutions to stem the national opioid public health crisis and offer new hope for individuals, families, and communities affected by the devastating crisis.

Since its inception, the NIH HEAL Initiative Research Plan[50] has provided an overarching vision, concrete goals, and milestones that are built around two overarching priorities: 1) enhancing pain management, and 2) improving the prevention and treatment for opioid misuse and addiction. The HEAL Initiative leverages expertise from almost every NIH Institute and Center to approach the crisis from all angles and disciplines, and across the full spectrum of research from basic research to implementation science. In consultation with a broad range of stakeholders, NIH identified six research focus areas that fall within the Initiative's two overarching priorities. Each focus area, as well as their aims, are briefly summarized below:

Enhancing Pain Management with Non-Addictive Therapies

> *Preclinical and translational research in pain management:* More effective, non-addictive, therapies for pain are needed, but limitations in current animal models, changes in biopharmaceutical industry business focus, and perceived regulatory and reimbursement concerns have posed obstacles to research. Through a suite of targeted research efforts, the HEAL Initiative will accelerate the discovery and preclinical and translational development of new medications and devices to treat pain.

[50] https://heal.nih.gov/about/research-plan

Clinical research in pain management: The HEAL Initiative supports research to evaluate the safety and efficacy of innovative, non-addictive, therapies for pain management in a number of different pain conditions. These clinical trials will help inform evidence-based guidelines for the treatment of pain with non-opioid therapies and reduce the risk of prescription opioid medications.

Improving Prevention and Treatment for Opioid Misuse and Addiction:

New strategies to prevent and treat opioid addiction: The HEAL Initiative supports research focused on preventing individuals with low-severity opioid use disorder (OUD) from developing a more severe OUD, building strategies to keep people in medication treatment for opioid addiction for long enough to support long-term recovery, understanding the role of sleep dysfunction in OUD and recovery, preventing at-risk adolescents from developing OUD, and exploring collaborative care for people with OUD and mental health conditions.

Translation of research to practice for the treatment of opioid addiction: There are multiple effective evidence-based treatments and programs for OUD, but most Americans at risk for or with OUD do not receive appropriate treatment for their disorder. To better understand how promising evidence-based strategies and treatments might help more people with OUD, the HEAL Initiative will deploy a suite of implementation science efforts to test the integration of evidence-based interventions in a multitude of settings.

Novel medication options for opioid use disorder and overdose: Expanded treatment options for OUD are needed to promote long-term recovery in more patients. The HEAL Initiative will accelerate the development of novel medications and devices to treat all aspects of the opioid addiction cycle, including progression to chronic use, withdrawal symptoms, craving, relapse, and overdose.

Enhanced outcomes for infants and children exposed to opioids: The best approaches to address the medical and social needs of children with neonatal abstinence syndrome and neonatal opioid withdrawal syndrome, which increased fivefold among infants covered by Medicaid in 46 states, is critical for the future health of the country.

The HEAL Initiative has established extensive collaborations across NIH. Staff from nearly every NIH Institute and Center manage the program through fully integrated teams of research program experts. A Multi-Disciplinary WG, made up of research experts from the private sector, patient and academic research community, and multiple NIH advisory councils, provides input to the HEAL and NIH leadership to help ensure research meets the bold, trans-NIH goals set for the initiative.

Scientific Highlights:

NIH intends to maximize the availability of publications and the sharing of underlying data generated through the HEAL Initiative research projects. By making publications and the

primary data behind them available as rapidly as possible, the HEAL Initiative promotes dissemination of new knowledge, enhances reproducibility, and accelerates the ability of researchers to build upon the Initiative's research to make new discoveries. In 2019, over 350 research projects were awarded under the HEAL Initiative within the six research focus areas. Twelve NIH ICOs lead 25 research programs that support a diverse community of researchers working across the research spectrum. Below is a summary of the research programs that fall within each of the six research focus areas and the challenges that they seek to address.

Preclinical and translational research in pain management

The overreliance on prescription opioids for the management of chronic pain conditions, despite limited effectiveness among some patients, has contributed to the recent epidemic of deaths due to opioid overdose. To address this challenge, the National Institute of Neurological Disorders and Stroke (NINDS) leads efforts to accelerate the scientific discovery and validation of novel treatment targets for acute and chronic pain conditions.[51] The newly created Preclinical Screening Platform for Pain aims to further identify and profile non-addictive therapeutics for pain conditions,[52] while the NCATS has established a complementary in vitro screening platform for testing of therapeutic candidates for pain in non-animal models.[53] Translating these discoveries requires more accurate research models to help understand how potential new drugs will affect humans. To this end, research led through NCATS facilitates novel human cell-based screening platforms, pharmacological probes, and pre-clinical drug development.[54] Further efforts aim to advance optimization and early development of promising small molecules and biologic agents to advance low-risk treatment options for chronic pain toward clinical development.[55] NINDS, NIBIB, and the Common Fund foster the development of next-generation medical devices to diagnose and treat pain,[56] including implanted devices, such as electrodes, and noninvasive targeted stimulation of nerve cells and regions of the brain associated with pain perception.

Clinical research in pain management

Advancing clinical research on pain management is a core goal of the HEAL Initiative. The Early Phase Pain Investigation Clinical Network (EPPIC-Net), led by NINDS, provides proof-of-concept clinical testing of potential biomarkers and new treatments to help identify specific pathways or mechanisms that hold promise for future therapeutic development.[57] EPPIC-Net also interfaces with the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) led Back Pain Consortium, which studies how people with different types of back pain respond to specific interventions.[58] The Pain Management Effectiveness Research Network clinical trials, which leverage the infrastructure of NCATS Trial Innovation Network, are designed to evaluate the effectiveness of pharmacologic and nonpharmacologic therapies for a broad array of acute and chronic pain conditions. This program is closely aligned with the high-priority recommendations of the Federal Pain Research Strategy and supports implementation of

[51] https://heal.nih.gov/research/preclinical-translational/novel-targets
[52] https://heal.nih.gov/research/preclinical-translational/screening-platform
[53] https://ncats.nih.gov/heal
[54] https://heal.nih.gov/research/preclinical-translational/novel-drugs-screening-platforms
[55] https://heal.nih.gov/research/preclinical-translational/optimization-non-addictive-therapies
[56] https://heal.nih.gov/research/preclinical-translational/discoveries-into-devices
[57] https://heal.nih.gov/research/clinical-research/eppic-net
[58] https://heal.nih.gov/research/clinical-research/back-pain

the recommendations of the Pain Management Best Practices Inter-Agency Task Force.[59] It will be of particular importance to determine which evidence-based strategies are most effectively implemented in health systems. Pragmatic trials led by the National Center for Complementary and Integrative Health (NCCIH) will help determine the effectiveness of multiple non-opioid interventions for treating pain and assess the impact of implementing interventions or guidelines.[60] Similarly, NIDDK coordinates an integrated approach to pain and opioid use in hemodialysis patients to identify novel risk factors in this population, which has the potential to reduce the rate of opioid prescription and opioid use and address related issues, such as depression, anxiety, and pain.[61]

New strategies to prevent and treat opioid addiction

Expanding the evidence of what treatments work in the real world is a priority of the HEAL Initiative, which requires prevention measures that incorporate the specific challenges of opioids. For example, there is an urgent need to identify effective approaches to treat people who have an opioid use disorder and co-occurring mental health conditions, especially in primary care settings. HEAL-supported research led by National Institute of Mental Health (NIMH) utilizes the collaborative care model to determine its usefulness in treating this population.[62] Studies led by NIDA focus on other high-risk populations, including older adolescents and young adults, that require strategies and settings that can identify and reach those at risk, such as health care, justice, school, and child welfare systems.[63] Understanding whether sleep deficiency contributes to the overuse of opioids and addiction could open avenues for novel prevention and treatment approaches. As a result, the NHLBI leads basic and clinical research to identify the behavioral and molecular mechanisms that directly connect sleep to the biological underpinnings of OUD.[64] Additional prevention research carried out through the National Drug Abuse Treatment Clinical Trials Network brings together medical and specialty treatment providers, researchers, and patients to test interventions aimed at stopping the progression from risky opioid use to more severe OUD,[65] and supports research to define the optimal length of medication treatments for OUD approved by the FDA.[66]

Translation of research to practice for the treatment of opioid addiction

The integration of evidence-based intervention into routine clinical usage requires focused efforts. The HEAL Initiative utilizes implementation studies to test the systematic uptake of research findings into routine practice. For example, NIH and the Substance Abuse and Mental Health Services Administration (SAMHSA) launched the HEALing Communities Study to investigate how tools for preventing and treating opioid misuse and OUD are most effective at the local level.[67] The goal of the study is to reduce opioid-related overdose deaths by 40 percent over the course of 3 years. NCCIH-led projects will also be carried out in the context of treatment services that SAMHSA provides for OUD and will layer additional research into state

[59] https://heal.nih.gov/research/clinical-research/pain-management-research
[60] https://heal.nih.gov/research/clinical-research/prism
[61] https://heal.nih.gov/research/clinical-research/hemodialysis
[62] https://heal.nih.gov/research/new-strategies/optimizing-collaborative-care
[63] https://heal.nih.gov/research/new-strategies/at-risk-adolescents
[64] https://heal.nih.gov/research/new-strategies/sleep-dysfunction
[65] https://heal.nih.gov/research/new-strategies/prevent-progression
[66] https://heal.nih.gov/research/new-strategies/duration-retention-discontinuation
[67] https://heal.nih.gov/research/research-to-practice/healing-communities

efforts to expand access to evidence-based treatment and recovery support services, including evidence-based behavioral interventions.[68] Additional NIDA-led efforts expand effective treatment and care in partnership with local and state justice systems and community-based treatment providers for people with opioid use disorder who pass through the criminal justice system.[69]

Novel medication options for opioid use disorder and overdose
To comprehensively address opioid addiction, the HEAL Initiative supports the development of new medications to treat all aspects of the opioid addiction cycle. Existing medications effectively reduce illicit opioid use when they are provided at a sufficient dose and patients adhere to their treatment plan, but not all patients respond to these medications. Growing knowledge of the neurobiology of opioid addiction has helped researchers to identify novel molecular targets and new ways of modifying brain circuits that may produce more effective and safer treatments for opioid use disorders.[70] NIDA and National Institute of Allergy and Infectious Disease (NIAID) lead novel approaches in development, including vaccines that recruit the body's immune system to prevent opioids from entering the brain. This approach has already shown great promise in animal studies.[71]

Enhanced outcomes for infants and children exposed to opioids
To best inform clinical care for infants born with opioid withdrawal syndrome, the HEAL Initiative supports an expansion of the Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome program, led by the NICHD, to assess both drug-free treatment approaches and currently used medications. The effects of early exposure to opioids on infant and child development are unknown, and therefore complementary efforts through NIDA-supported research are critical to help predict and prevent risk for future substance use, mental disorders, and other behavioral and developmental problems.[72]

Next Steps:
The HEAL Initiative's comprehensive approach to addressing the opioid epidemic includes concrete steps toward reducing the impact of opioid abuse on communities. Research supported through the Initiative is working to discover new, safer treatment options for pain management in order to improve quality of life and reduce the number of people exposed to the risks of opioids. Additionally, a series of highly focused studies will expedite the development of therapies to treat OUD and reverse overdose, including promising prevention strategies and evidence-based treatment in multiple settings, including primary and emergency care, the criminal justice system, and other community settings, and in communities highly affected by the opioid crisis.

In the short term (within three to five years), a few of the HEAL research investments are expected to deliver:

[68] https://heal.nih.gov/research/research-to-practice/brim
[69] https://heal.nih.gov/research/research-to-practice/jcoin
[70] https://heal.nih.gov/research/medication-options/focusing-development
[71] https://heal.nih.gov/research/medication-options/immunotherapies
[72] https://heal.nih.gov/research/infants-and-children/healthy-brain

- Implementation strategies demonstrated to significantly increase initiation of medication assisted treatment and retention in treatment beyond six months, and decrease rates of opioid addiction and overdose death;
- A clinical trials network poised for the rapid testing of new, non-addictive, pain therapies;
- New evidence-based approaches to inform previous practice-based approaches and improve care for infants with neonatal opioid withdrawal syndrome;
- Evidence for the non-pharmacological management of multiple acute and chronic pain conditions.

In the longer-term (over five years), HEAL will deliver:

- Pharmaceutical programs leading to 15 Investigational New Drugs (INDs) and Investigational Device Exemptions (IDEs), with the goal of 5 New Drug Applications (NDAs) or 510(k) premarket approvals for devices submitted to the FDA for novel medications to treat withdrawal, craving, and relapse;
- A pipeline of novel non-opioid therapies that can be further developed and tested for the treatment of acute and chronic pain;
- Understanding of the lasting effects of early exposure to opioids on children and young adults.

Next Generation Researchers Initiative: Investing in the Future of the Biomedical Workforce

The NIH has long recognized that the most critical assets in the biomedical research enterprise are the scientists who comprise its workforce. The biomedical research enterprise relies upon a pipeline of highly trained investigators to convey new insights, develop innovative ideas, and advance the translation of scientific research into improved health for all.

In September 2017, with support from the 21st Century Cures Act (P.L. 114-255), the NIH launched the Next Generation Researchers Initiative (NGRI).[73] This initiative aims to bolster opportunities for early-stage investigators (ESIs), those within 10 years of completing postgraduate clinical training or their highest advanced research degree. Applications from ESIs, like those from all new investigators, are given special consideration during peer review as well as at the time of funding consideration.

Through this initiative, NIH ICOs prioritize funding for ESIs[74] and track the impact of funding decisions for ESIs to ensure that this new strategy is effectively implemented. As a result of this initiative, NIH has substantially increased support for ESIs – from less than 600 ESIs in FY 2013, to 1,287 in FY 2018, and 1,316 in FY 2019. As part of NGRI, NIH is also developing methods to identify and support meritorious investigators (new or established) who are at risk for losing all NIH funding and who do not have significant research support from other sources.

NIH will continue to incorporate guidance from the ACD NGRI WG, coordinated by the OD, and the National Academies of Sciences, Engineering, and Medicine (NASEM) report "The Next Generation of Biomedical and Behavioral Sciences Researchers: Breaking Through"[75] in the future design, testing, implementation, and evaluation of policies and programs to enhance the success of the next generation of talented biomedical researchers. To address concerns raised in the NASEM report, NIH will continue to collect and analyze workforce related data to assess workforce trends. To this end, NIH published a report on trends in early stage, new, and established investigator demographics from 2009 and 2016.[76]

NIH currently has several successful programs to support ESIs and will continue to expand upon them, including the:

- NIH Director's New Innovator Award Program (DP2)
- Maximizing Investigators' Research Award (R35)
- NIH Pathway to Independence Awards (K99/R00)
- Director's Early Independence award (DP5)
- High Priority, Short-Term Project/Bridge Awards (R56)

In response to the ACD NGRI Workgroup Report recommendation, "2.1: Expand Pathways for funding ESIs through programs that do not require preliminary data," NIH plans to issue an

[73] https://grants.nih.gov/ngri.htm
[74] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-101.html
[75] https://www.nap.edu/catalog/25008/the-next-generation-of-biomedical-and-behavioral-sciences-researchers-breaking
[76] https://www.ncbi.nlm.nih.gov/pubmed/29920223

award in honor of the late Stephen I. Katz, M.D., Ph.D, Director of NIAMS from 1995-2018, who exhibited a profound dedication to mentoring the next generation of scientists. As described in a recent update to the ACD,[77] this new ESI award will be for investigator-initiated R01s; will not allow preliminary data; will support a change in research direction for the PI; and will provide for five years of funding.

NIH will continue to analyze the impact of NGRI policies on women and individuals from nationally underrepresented backgrounds in the NIH portfolio. Several sources of data show modest improvements in the representation of women in the biomedical research pipeline, but underrepresentation of women at faculty career levels remains a persistent issue. For example, an investigation of the gender makeup of the NIH funded research workforce found that female scientists are more likely than their male counterparts to be in the trainee/fellow postdoctoral and career development (K)-awardee pools and are less likely to be in the RPG and R01-equivalent awardee groups.[78] Although ESIs and new investigators (NIs) include a higher proportion of underrepresented minorities, Hispanics, and women than experienced investigators, the share of funding awarded to ESIs and NIs declined between 2009-2016, suggesting these populations may not be well supported.[79] NIH has developed and implemented a range of approaches to address these challenges:

- In FY 2018, NIH implemented automatic extensions of ESI status for childbirth for one year within the ESI period.[80]
- In FY 2018, NIH strengthened and clarified the NRSA parental leave policy to continue stipends during parental leave. [81]
- For many years, NIH has offered support for investigators with high potential to re-enter an active research career after an interruption for family responsibilities or other qualifying circumstances. [82]
- In FY 2018, NIH issued a Guide Notice describing its interest in diversity, stating that "NIH encourages institutions to diversify their student and faculty populations to enhance the participation of individuals from groups that are underrepresented in the biomedical, clinical, behavioral and social sciences."
- In FY 2020 NIH updated its interest-in-diversity Guide Notice by expanding the definition of socio-economic disadvantage to be more inclusive and diverse.[83]
- Many ICs are piloting new programs to enhance workforce diversity. [84] [85]
- In FY 2020, NIH will approve an automatic extension of one year for childbirth within the 4-year K99 eligibility window.[86]

[77] https://acd.od.nih.gov/documents/presentations/12122019NextGen.pdf
[78] Acad Med. 2016 August; 91(8): 1164–1172. doi:10.1097/ACM.0000000000001209
[79] FASEB J. 2018; 32:6410–6422. doi: 10.1096/fj.201800639
[80] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-235.html
[81] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-154.html
[82] https://grants.nih.gov/grants/guide/pa-files/pa-18-592.html
[83] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-031.html
[84] https://grants.nih.gov/grants/guide/pa-files/PAR-18-813.html
[85] https://grants.nih.gov/grants/guide/pa-files/PAR-18-814.html
[86] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-011.html

NIH remains strongly committed to the goals of NGRI to fund more early-career investigators, protect and retain meritorious at-risk scientists, and enhance the diversity of the biomedical research workforce.

Diversity and Inclusion Initiatives at NIH

ICOs Involved:
NIH-wide
Office of Extramural Research (OER)
Office of Research on Women's Health (ORWH)
National Institute on Minority Health and Health Disparities (NIMHD)
Office of Scientific Workforce Diversity (OSWD)
Office of Equity, Diversity and Inclusion (EDI)
Office of Human Resources (OHR)

Growing and Maintaining a Diverse Biomedical Workforce
Through a comprehensive approach, NIH is working to develop a diverse, skilled biomedical workforce for the future. Increasing representation and diversity in both the NIH intramural and extramural communities is a key goal of training, career development, and workforce-related programs. The Diversity Program Consortium is a trans-NIH program funded by the NIH Common Fund and coordinated by the NIGMS to bring together institutions to engage a more diverse field of individuals at the student, faculty, and institutional levels. This program is developing, implementing, assessing, and disseminating innovative, effective approaches to training and mentoring, with the ultimate goal of engaging a more diverse field of individuals in biomedical research careers. The NIH Distinguished Scholars Program works to build an inclusive community within the NIH Intramural Research Program by providing mentoring and professional development training to yearly cohorts of investigators with diverse backgrounds. The Future Leaders Research conference offers career development opportunities for diverse early-career researchers to share their scientific work and learn from NIH leaders and investigators. Additionally, OD, through the work of the Chief Officer for OSWD, is enhancing transparency and accountability in scientific workforce diversity metrics through a trans-NIH results-based accountability network, online data and reporting tool, and formalization of a trans-NIH committee devoted to this initiative.

In addition, the NIH Working Group on Women in Biomedical Careers (WgWBC) is a trans-NIH group composed of senior leadership of NIH ICOs. This trans-NIH effort considers and addresses barriers for women in science by developing innovative strategies including policies and funding initiatives. The strength of the group lies in its trans-NIH approach, which provides a framework for influence, collaboration, and action across the agency. Specifically, the WgWBC is chartering innovative strategies to promote recruitment, entry, retention, and sustained advancement of women in biomedical research careers. Current efforts underway include the development of a portfolio of initiatives to address the underrepresentation of women in biomedical careers. Together, these programs complement ongoing or other nascent programs at the NIH to enhance diversity and comprise a comprehensive approach that targets both individual investigators and institutional change. These initiatives are expected to be released in FYs 2020 and 2021. In addition, the Women of Color (WOC) committee[87] of the WgWBC created a Women of Color Research Network (WoCRN) on the LinkedIn platform to provide women of color and supporters of their advancement in the biomedical sciences with information about the NIH grants process, advice on career development, and a

[87] https://womeninscience.nih.gov/about/committees.asp#womenofcolor

venue or forum for networking and sharing information. With the addition of two regional chapters in of WoCRN recent years, the ORWH and the WgWBC continue to improve upon the content and grow the network. Moving forward, the WgWBC will periodically review policies and progress related to NIH childcare, the NIH intramural workforce concerning gender, and work-life integration issues.

The WgWBC continues to convene thought leaders to consider these issues and propose plausible solutions, thus serving as a strong framework by which change can occur. Relatedly, the ORWH is co-sponsoring a National Academies consensus study on this topic that will be concluded and published in early 2020. The report will provide recommendations for funding agencies, institutions, and other stakeholders to drive progress for women in Science, Technology, Engineering, Mathematics, and Medicine (STEMM) careers. This report will inform future directions for the ORWH and for the NIH WgWBC to propose systemic approaches including policy, institutional transformation programs, and interagency and private-public partnerships.

The ORWH within the OD, the NIH WgWBC, the OD OER, and other NIH ICO leadership and staff have developed and implemented a constellation of initiatives and programs to enhance work-life integration for the scientific workforce on behalf of the agency as a means to maintain a diverse biomedical workforce. Approaches in the NIH extramural community include targeted support for investigators with high potential to re-enter an active research career after an interruption for family responsibilities or other qualifying circumstances. The NIH has also strengthened the parental leave policy on National Research Service Awards (NRSAs). The revised policy allows for the recipients, who are predoctoral and postdoctoral fellows, to continue to receive their stipends from their awards for up to eight weeks during their parental leave. Another key action has been the automatic extension of Early-Stage Investigator status for childbirth, which extends the period during which R01 applications from these investigators are given appropriate consideration for the investigator's less extensive research experience compared to senior investigators. An update to the NIH Support for Conferences and Scientific Meetings requires that applicants "describe plans to identify resources for childcare and other types of family care at the conference site to allow individuals with family care responsibilities to attend."

NIH has also implemented a multitude of policies and programs to address these challenges for those working at NIH. To ensure effective communication about the programs available, the Office of Research Services supports a publicly accessible website that describes the on-site childcare facilities and other resources available to NIH employees, intramural trainees, and contractors. The NIH Office of Human Resources has implemented a range of support tools, including a leave bank program for NIH employees to have access to paid medical leave if they or a family member become sick or for the birth of a child. Specific policies and programs for the NIH intramural community developed by the Office of Intramural Research within the OD include paid parental leave extension for NIH intramural trainees from six to eight weeks. In addition, the OD provides for tenure-clock modification for NIH intramural scientists that automatically incorporates an additional year to accommodate family leave, and the "Keep the Thread" program, an accommodation program for intramural postdoctoral fellows that offers flexible schedule options and part-time work options. Through all of these approaches, both

within and outside the agency, NIH is investigating ways to continue to develop work-life integration policies that will ensure a competitive and diverse workforce for the biomedical research enterprise now and in the future.

The NIH Intramural Loan Repayment and Undergraduate Scholarship Programs offer financial incentives along with other benefits to attract highly qualified physicians, nurses, and scientists into careers in biomedical, behavioral, and clinical research as employees of NIH. The Intramural Loan Repayment Program (ILRP), housed in the Office of Intramural Research, repays outstanding eligible educational debt for NIH employee postgraduates. In return, participants enter into a contractual agreement to conduct qualified research in one of several areas as identified by the ILRP and coinciding with the NIH mission. The Undergraduate Scholarship Program (UGSP), also housed in the Office of Intramural Research, offers competitive scholarships to exceptional undergraduate students from financially disadvantaged backgrounds. Awardees must be committed to biomedical, social science, or behavioral health-related research career paths. In exchange for each year or partial year of scholarship funding, UGSP award recipients are contractually obligated to participate in a 10-week summer internship and 1 year as a full-time paid employee of the NIH Intramural Research Program. The goal of these programs is to continue to build and maintain a diverse biomedical workforce.

NIH Efforts to End Harassment and Cultivate A Culture of Respect

NIH does not tolerate harassment of any kind, including sexual harassment, whether it is within the agency, at research organizations that receive NIH funding, or anywhere else NIH-funded activities are conducted. The OD is bolstering policies and practices to foster a culture of respect wherever NIH research activities are conducted, and ensure sexual harassment is not tolerated or ignored. Over the last year, NIH leadership has been heavily focused on this issue, with guidance from the NIH Anti-Harassment Steering Committee, coordinated by the OD, and recommendations developed by the ACD Working Group on Changing the Culture to End Sexual Harassment. (See discussion of the Working Group's recommendations earlier in this narrative.) These actions aim to create a paradigm shift in the scientific culture wherever NIH research activities take place to eliminate sexual harassment and enhance contributions by women and others to scientific advancements.

Through a multi-faceted campaign, NIH has taken actions to address harassment for all NIH staff, including the launch of a new, central website on all NIH anti-sexual harassment activities that comprehensively outlines NIH policies, practices, and initiatives. NIH has also issued two new policies that apply to the entire NIH community, including contractors and trainees/fellows, and focus on preventing harassment and inappropriate conduct and addressing personal relationships in the workplace. NIH has also developed a new training module to inform the NIH community of the anti-harassment policy and expanded the existing NIH Civil Program to establish a centralized, independent office to consistently address allegations of harassment, manage related administrative inquiries, and track and report data regularly to the Anti-Harassment Steering Committee and annually to the NIH community. NIH also established a new centralized process for managing reports of harassment and subsequent administrative inquiries for both NIH staff and the extramural community. In early 2019, a survey was disseminated to all NIH staff, including contractors and fellows, to assess NIH workplace climate and harassment, with the goal of implementing programs to address sexual harassment in

the workplace and set a baseline to evaluate their effectiveness to ensure effective policies and successful implementation.

NIH efforts on harassment at recipient institutions include the launch of a new, central website on its anti-harassment activities that comprehensively outlines NIH policies, practices, and initiatives as a funding agency. NIH has reminded applicants of the requirements for applicant and recipient research institutions to ensure safe and healthful working conditions for their employees and foster work environments conducive to high-quality research. NIH continues to require that institutions notify the NIH if the institution takes an administrative or disciplinary action against its employee(s) that affects the ability of the employee(s) to continue as principal investigator (PI) or other senior key personnel on an NIH award. NIH can take a variety of actions including suspension or termination of the grant if the proposed alternative arrangements are not acceptable. Several different means of communication have been used to publicize these efforts and ensure that NIH expectations are understood and met.

NIH will continue working with stakeholders to develop best practices for establishing safe, diverse, and inclusive research environments. NIH is a member of the subcommittee of the National Science and Technology Council (NSTC) Joint Committee on Research Environments. Safe Inclusive Research Environments (SIRE) has representation from a number of Federal departments and agencies and builds upon previous and current interagency or agency-specific efforts. One goal of the committee is to coordinate and facilitate sharing of best practices.

Foreign Influence on Research Integrity

NIH research is built on the bedrock principles of scientific excellence, unassailable integrity, and fair competition. The U.S. biomedical enterprise sets the standard for discovery and innovation excellence for the world. This is made possible because the overwhelming majority of researchers participating on NIH grants, whether U.S. or foreign-born, are honest contributors to the advancement of knowledge that benefits us all. NIH recognizes the importance of scientific collaborations, including those involving international institutions, to advance its mission. Yet, there are threats to the integrity of the biomedical research enterprise, including the failure by some researchers at NIH-funded institutions to disclose contributions of resources from other organizations; diversion of intellectual property produced by NIH-supported biomedical research to other entities, and sharing of confidential information by peer reviewers with others or otherwise attempting to influence funding decisions.

NIH's Overall Approach

NIH's commitment to tackling these important challenges is reflected in a variety of recent actions, including the convening of an NIH ACD WG for Foreign Influences on Research Integrity.[88] Acting on ACD recommendations, NIH is increasing awareness with institutions on their need to disclose all affiliations and other support, mitigate and prevent risks, and work with federal partners on issues of research security and integrity. Moreover, NIH is clarifying long-standing policies that require disclosure of all other support (including support from foreign entities), foreign components, and financial conflicts of interest.

Partnerships with other federal agencies, professional organizations, and institutions have led to extensive discovery about the nature of the threats, actions by the relevant institutions against certain investigators, referrals to the HHS Office of Inspector General (OIG), and institutional implementation of additional internal systems control measures. NIH's efforts to raise awareness have prompted several institutions to perform internal reviews that revealed undisclosed conflicts of interest, which the institutions self-report to NIH.[89]

NIH will continue to actively partner with other federal departments and agencies to address concerns related to undue foreign influence on the biomedical research enterprise. These federal partners include the Central Intelligence Agency, Federal Bureau of Investigation, OIG, Department of Defense, Department of State, Department of Energy, and the National Science Foundation (NSF). Notably, the NSF recently released report by the independent science advisory group JASON titled "Fundamental Research Security."[90] Research agencies across the federal government are coordinating to address the challenges outlined in the report. NIH will also continue engaging the HHS' Office of National Security and the NIH Counterintelligence and Insider Threat program to address security issues appropriately for the protection of all NIH-funded assets, including data.

[88] https://www.acd.od.nih.gov/working-groups/foreign-influences.html
[89] https://cancerletter.com/articles/20191220_2/
[90] https://www.nsf.gov/news/special_reports/jasonsecurity/JSR-19-2IFundamentalResearchSecurity_12062019FINAL.pdf

NIH participates in the White House Office of Science and Technology Policy (OSTP) Joint Committee on the Research Environment (JCORE), with several subcommittees co-chaired by NIH. The Rigor and Integrity subcommittee will focus on areas to promote baseline policies across Federal agencies and work with external stakeholders to share recommendations and best practices. The Research Security subcommittee will focus on coordinating Federal efforts to effectively communicate and provide outreach to academic and research institutions, develop guidance and best practices for academic and research institutions, and standardize financial conflict of interest and commitment disclosure requirements and enforcement behaviors that affect the safety and inclusivity of our research environments.

NIH has also been working to bolster its own internal controls and increasing awareness among NIH staff. The NIH Office of Intramural Research added guidance to the Intramural Source Book to help PIs navigate international interactions and avoid inappropriate foreign influences on their research. The goal is to enable continuing and future interactions among NIH scientific staff and foreign scientists under circumstances where the NIH PI and the NIH as an institution are satisfied that the circumstances of such interactions do not allow undue foreign influence on NIH-supported research.

Extramural Institutions and Grantee Compliance

NIH continues to strongly encourage universities to look closely at their organizations to mitigate unscrupulous practices by individuals and entities that aim to capitalize on the collaborative nature of the U.S. biomedical enterprise. Regular communications to the extramural community over the last several years have focused on protecting the integrity of U.S. biomedical research and the imperative to inform NIH of any foreign support. These communications have included several notices and statements to the community (most recent notice on other support and foreign components[91]), including the unprecedented step of the NIH Director issuing a letter to officials at approximately 10,000 recipient institutions.[92] This letter informed the research community that the agency is aware that some foreign entities have mounted systematic programs to influence NIH-supported researchers and peer reviewers, as well as to take advantage of the long tradition of trust, fairness, and excellence of NIH-supported research activities.

NIH has contacted more than 75 institutions regarding specific scientists who may have failed to disclose substantial foreign research support or financial conflicts of interest or who may have engaged in substantial breaches of peer review integrity. This outreach has led to referrals to the OIG, communications with FBI, disciplinary actions by the relevant institutions (including terminations or resignations), revisions of grant terms, and new efforts on the part of institutions to enhance oversight and security of their research operations.

Furthermore, NIH regularly communicates with grantees to provide training and compliance support for issues involving financial conflict of interest requirements at NIH-led conferences such as the NIH Regional Seminars. NIH also communicates this information through professional organizations such as the Society for Research

[91] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-114.html
[92] https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-protecting-integrity-us-biomedical-research

Administrators, and the National Council of University Research Administrators. There have been a number of special meetings involving these groups and others to address the recent concerns on foreign influence. In addition, NIH has recently updated an online training module[93] on Financial Conflict of Interest as a resource for both NIH staff and the extramural community. NIH's outreach and engagement have facilitated extensive faculty outreach at research organizations as well as led to developing and sharing best practices.

One indication that these communication strategies are proving to be successful is a report on *Actions Taken by Universities to Address Growing Concerns about Security Threats and Undue Foreign Influence on Campus*,[94] issued by the American Association of Universities and the Association of Public and Land-Grant Universities, and updated in April 2019. This report shares practices that universities are employing to "ensure the security of research, protect against intellectual property theft and academic espionage, and prevent actions or activities by foreign governments and/or other entities that seek to exert undue foreign influence or that infringe on core academic values."

NIH's collaborations with other federal agencies and outreach to the research community have led to several research institutions terminating or accepting the resignations of scientists due to conflicts of interest with foreign institutions.[95,96,97] One case led to an outside institution paying $5.5 million to resolve allegations that it violated the False Claims Act by submitting federal grant applications and progress reports to the NIH in which it failed to disclose foreign government grants that funded two researchers.[98]

Protecting Peer Review Integrity

In recent years, NIH has taken numerous steps to protect the integrity of the peer review process. All participants in the NIH peer review system are responsible for promoting integrity. Maintaining integrity in the peer review process – including keeping application data confidential and secure – is essential for ensuring robust exchange of scientific opinions and evaluations without fear of reprisal; protecting trade secrets and other proprietary, sensitive and/or confidential information; providing reliable input to NIH about which research projects it should support; and maintaining public trust in science.

In addition to issuing several Guide Notices[99] and blogs[100] on the confidentiality and integrity of peer review, NIH has referred several cases to the HHS OIG for consideration of debarment or suspension and has removed the violating individuals from peer review service. Also, in 2018, reviewer conflict-of-interest certifications were converted to a completely electronic format,

[93] https://nexus.od.nih.gov/all/2018/12/03/new-financial-conflict-of-interest-training-module-available/
[94] https://www.aplu.org/members/councils/governmental-affairs/Effective-Sci-Sec-Practices-What-Campuses-are-Doing.pdf
[95] https://www.sciencemag.org/news/2019/04/exclusive-major-us-cancer-center-ousts-asian-researchers-after-nih-flags-their-foreign
[96] https://www.sciencemag.org/news/2019/05/emory-ousts-two-chinese-american-researchers-after-investigation-foreign-ties
[97] https://cancerletter.com/articles/20191220_2/
[98] https://www.justice.gov/usao-wdmi/pr/2019_1219_VARI
[99] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-115.html
[100] https://nexus.od.nih.gov/all/2019/06/25/breaches-of-peer-review-integrity/

enabling a more thorough assessment of compliance across the agency and in cases of individual breaches.

The NIH OER has expanded its internal training for NIH Scientific Review Officers (SROs) to raise their awareness of integrity concerns. OER held three well-attended, interactive training sessions on peer review integrity in the last year. These events covered case studies largely based on actual events and stimulated lively discussion of the best course of action in each scenario. NIH is also working to implement recommendations from the NIH Advisory Committee to the Director on Foreign Influences on Research Integrity that focus on peer review integrity.

NIH continues to explore new technologies and ideas to protect the integrity and security of the peer review process. For example, a new electronic forensics dashboard is being developed to assist the Office of the Director in identifying data needed to investigate possible peer review integrity violations. Other electronic systems are being enhanced, including those that investigators use to submit applications and peer reviewers use to access applications for evaluation. Finally, policies for permissions to access certain information such as the preliminary score matrix are being re-assessed, and a new application is being developed to more efficiently implement those rules. Taken together, these efforts to communicate internally and externally, as well as modernize controls, are raising the profile on peer review integrity concerns and reducing risks.

Big Data and the Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) Initiative

Rapid advances in data generation, computing, networking, and algorithms, such as artificial intelligence (AI), are intertwined in a newly evolving digital infrastructure. High throughput data generation is driving the need for advances in information-based algorithms and memory-rich computers to interpret data in new ways. Today, biomedical data is measured in petabytes and comprises data types ranging from DNA sequences to wearable sensor-generated outputs, like heartrate. This increase in pace, scale, and complexity of data, which can be used to understand and alleviate diseases, underpins the notion of "big data" for biomedical research. Researchers working with "big data" envision a biomedical research enterprise in which data and information generated in the field, laboratory, and clinic are processed and analyzed quickly in real-time and readily shared. In addition to data generation, tools, and technologies like AI are creating opportunities to maximize the use of these data. Making these data findable, accessible, interoperable, and reusable (FAIR) is a major goal for NIH, and the STRIDES Initiative is enabling through storage of rich datasets, advanced computational infrastructure, tools, and professional services. The Office of Data Science Strategy (ODSS)[101] is leading a cross-agency effort with NIH institutes, centers, and offices to address complex challenges and build solutions in a unified, economic, and sustainable way. A subset of those efforts, and programmatic examples from specific Institutes, Centers, and Offices, are included in this narrative.

In June 2018, NIH provided Congress a new roadmap to modernize the NIH-funded biomedical data ecosystem, the NIH Strategic Plan for Data Science.[102] The ODSS, created in October 2018 after a request in the Senate appropriations language, now leads and coordinates the NIH-wide efforts to implement the plan in consultation with the Scientific Data Council. Over 30 teams across NIH work on specific goals with visible outcomes, exemplified below.

Piloting FAIR

Common Fund New Models of Data Stewardship (NMDS) Initiative

Before ODSS was formed, NIH invested in the NMDS to learn how to harness and use big data to its fullest capacity. From FY 2017 to FY 2018, the Common Fund supported the NMDS program, an integrated set of activities that piloted new digital data management strategies. One initiative under NMDS was the NIH Data Commons Pilot Phase,[103] which explored new ways to store, access, and share biomedical data and associated tools in the cloud, so they were FAIR. The Data Commons Pilot Phase iteratively experimented with a set of key capabilities needed for datasets to operate and meet FAIR standards. Three different test case datasets from across NIH helped in setting policies, processes, and architecture for the Commons. The tools and best practices from the Data Commons Pilot Phase informed a broader trans-NIH data ecosystem strategy that is being planned through ODSS. The Common Fund will continue to test, evaluate, and refine a subset of deliverables from the Data Commons Pilot Phase in the development of the Common Fund Data Ecosystem (described below).

[101] datascience.nih.gov/
[102] datascience.nih.gov/sites/default/files/NIH_Strategic_Plan_for_Data_Science_Final_508.pdf
[103] commonfund.nih.gov/commons

Bringing Cloud Environments to Biomedical Research

The NIH STRIDES Initiative[104] is an ongoing effort that enables NIH to provide researchers cost-effective access to industry-leading cloud service providers (CSPs) for the storage of rich datasets, advanced computational infrastructure, tools, and professional services. ODSS, in close partnership with the NIH Center for Information Technology (CIT), is supporting and managing the STRIDES Initiative. The initiative reduces economic and technological barriers to accessing and computing on large biomedical datasets and aims to accelerate biomedical advances by providing discounts on STRIDES Initiative partner and professional services, training, and potential collaborative engagements. In the past year, NIH has co-located over 25 petabytes of high-value datasets and data resources to STRIDES CSPs. ODSS anticipates that by the summer of 2020, the amount of NIH-supported data in the cloud will be more than 50 petabytes. Data resources across NIH are supporting biomedical data in the cloud under STRIDES, including:

Common Fund Data Ecosystem (CFDE)

The Common Fund is supporting a coordinated effort among several data-generating programs to develop the CFDE,[105] where Common Fund datasets will be accessible and interoperable in a digital cloud environment. The CFDE will provide a framework for researchers to analyze data simultaneously from different and diverse datasets. During its initial development, the CFDE will work with four Common Fund datasets from the Gabriella Miller Kids First Pediatric Research (Kids First[106]), Genotype-Tissue Expression (GTEx[107]), Library of Integrated Network-based Cellular Signatures (LINCS[108]), and Human Microbiome Project (HMP[109]) programs. Starting this effort with four unique and complex datasets will allow for a deeper understanding of the issues around using and integrating diverse datatypes, identify specific needs for individual programs, and help with collaboration across programs to enhance data searching. Since Common Fund datasets are highly relevant to datasets supported by institutes and centers, the Common Fund is working with NHLBI, NHGRI, and the National Cancer Institute (NCI) to work toward broader interoperability. Working with STRIDES will enable proper data versioning and upkeep, as well as favorable pricing for cloud data storage and use. As CDFE learns best practices and new lessons, they will be applied to additional datasets from Common Fund programs.

Trans-Omics for Precision Medicine (TOPMed)

NHLBI's TOPMed program is designed to improve understanding of the fundamental biological processes that underlie heart, lung, blood, and sleep disorders. It includes whole genome sequences and other clinical and imaging data from a diverse population of more than 149,000 individuals participating in more than 80 studies, including the Framingham Heart Study and Jackson Heart Study. NHLBI data scientists are developing ways to make these data available to more researchers. Genomic data from the TOPMed program were made available to researchers through the NIH Data

[104] datascience.nih.gov/strides
[105] commonfund.nih.gov/dataecosystem
[106] commonfund.nih.gov/KidsFirst
[107] commonfund.nih.gov/GTEx
[108] commonfund.nih.gov/LINCS
[109] commonfund.nih.gov/hmp

Commons Pilot Phase, which helped guide the development of broader trans-NIH cloud computing strategies that are part of the NIH STRIDES initiative and in line with the NIH Strategic Plan for Data Science.

Sequence Data Delivery Project (NLM)
The National Library of Medicine's (NLM) Sequence Read Archive[110] (SRA) is the largest publicly available repository of next-generation genomic sequence data. Each month, more than 9 million records and more than 100,000 users access more than two petabytes of data. To improve access to these data and enable large-scale computational analysis for novel scientific discovery, NLM has uploaded all non-human publicly available SRA data to two commercial cloud platforms, Google Cloud and Amazon Web Services, as part of the STRIDES Initiative. Freed from the limitations of local storage and compute resources, any user is empowered to compute across the entire five-petabyte data corpus of public SRA data and metadata, which significantly expands the discovery potential and makes it possible to develop customized compute tools and methods. The public SRA data include genomes of viruses, bacteria, and nonhuman higher organisms, as well as gene expression data, metagenomes, and a small amount of human genome data that is consented to be publicly available (e.g., data from the 1000 Genomes Project[111]). The second phase of this effort will be to make all of SRA's controlled-access human genomic data available on both cloud platforms, with a higher level of security and oversight to ensure the protection of data from human samples or specimens, and the authorization and authentication of users of these data.

The STRIDES Initiative also supports other data resources, including components of NCI's Research Data Commons, parts of NHGRI's Analysis, Visualization, and Informatics Lab-space (AnVIL[112]), and some other NLM data resources in addition to the SRA. These large data resources present new opportunities and challenges in the development of algorithms, such as AI, that can work on petabyte-scale datasets. By leveraging the STRIDES Initiative, NIH and NIH-funded institutions can begin to create a robust, interconnected ecosystem that breaks down silos related to generating, analyzing, and sharing research data.

In addition to making accessible large data resources, such as those typically developed by research consortiums or broader NIH initiatives, NIH is equally committed to making heterogeneous datasets resulting from NIH investigator-initiated research more discoverable. For example, researchers may find themselves with a need to share data but unable to identify an appropriate data repository to do so. NIH is evaluating how "generalist" repositories might fill this gap through the pilot development of NIH Figshare,[113] an instance of the commercial Figshare generalist repository platform. The NIH Figshare instance will provide NIH with information to evaluate cost, usage patterns of data deposit, and data re-use to inform future implementation activities in enabling FAIR-data sharing.

[110] ncbi.nlm.nih.gov/sra
[111] internationalgenome.org/about/
[112] genome.gov/Funded-Programs-Projects/Computational-Genomics-and-Data-Science-Program/Genomic-Analysis-Visualization-Informatics-Lab-space-AnVIL
[113] Figshare is a generalist repository where users can make their research outputs available and citable in a searchable framework. Figshare is a part of the Digital Science, a for-profit company.

Unifying Authorization and Authentication
Many institutes, centers, and high-impact programs at NIH are developing data platforms for their research communities. One major current limitation is that data platforms are not using a unified authentication and authorization system, making trans-NIH data science discoveries difficult. Having an identity and access management (IAM) system will foster a connected data platform infrastructure (e.g., an "ecosystem"), improve cost, performance, accuracy, resolution, throughput, flexibility, and usability. ODSS is working closely with the CIT and NLM to build a single, unified, efficient, and secure authentication and authorization service that will provide researchers with access to data resources that the STRIDES Initiative CSPs host. To enable data-focused research, this year, NIH will develop a minimum viable product to provide authentication, authorization, auditing, and logging support for a common, federated experience for biomedical researchers to access NIH-funded data resources.

Data Archive (NIMH)
One of the many projects that will benefit from the new IAM system is the NIMH Data Archive (NDA).[114] The NDA houses human participant data from multiple repositories in a single database infrastructure. NDA makes data from different research projects as consistent as possible and allows other researchers access to those data for secondary analysis, methodology development, and tool development. NDA data include clinical/phenotypic, imaging, genomic, and other data from hundreds of thousands of research participants. Initially established to support autism research, NDA has grown into an informatics platform that contains several NIMH data repositories, including the National Database for Autism Research, the National Database for Clinical Trials related to Mental Illness, the Research Domain Criteria Database, and the NIH Pediatric MRI Data Repository. Additionally, this informatics platform supports other trans-NIH data repositories, such as the Adolescent Brain Cognitive Development Study, the Connectome Coordination Facility (CCF), the Osteoarthritis Initiative, and the National Institute on Alcohol Abuse and Alcoholism Data Archive. The NDA platform securely shares data, tools, methods, and provides a platform for secure analyses.

As NIH introduces these new platforms to the biomedical research communities, ODSS, the STRIDES team, and many others across NIH will work together to communicate processes and provide training and assistance to enable researchers, programs, and institutions with access to data storage and compute.

Advancing Clinical Research
As data generation and access to technologies increase, NIH researchers will have increased access to clinical data from EHR systems for research, making clinical research data collected for one study useful for other research endeavors. NIBIB has supported the development of one such resource:

A freely available multi-center database for critical care research (NIBIB)
Critical care patients undergo constant monitoring for the duration of their hospital stay that typically gets stored in a hospital's telehealth system. NIBIB-supported scientists

[114] nda.nih.gov/

have developed a publicly available intensive care unit (ICU) database (eICU Collaborative Research Database) that contains deidentified vital signs and lab measurements, their caretakers' notes, treatment plans, official diagnoses, and other data. The free database has been accessed and used in about 500 research papers. A recent impactful study utilized the database to develop an algorithm that could be used to predict whether patients would return to the ICU within a month.

Enhancing Connectivity of Clinical Research Resources

NIH is promoting the use of a specific health data standard, the HL7® Fast Healthcare Interoperability Resources® (FHIR®)[115] standard. To create a bridge between important EHRs and clinical research data, ODSS and NLM are supporting FHIR-enabled tools and technology applications. FHIR is a global industry standard for exchanging healthcare data electronically between information systems (such as EHR or clinical trial records systems) through an application programming interface (API). It's free, open, and designed to be quick to implement. NIH issued a Guide Notice on FHIR[116] to encourage NIH-funded investigators to explore the use of FHIR to capture, integrate, and exchange clinical data for research purposes and to enhance capabilities to share research data. NIH also published a Notice of Special Interest[117] to inform the small business community of NIH's interest in supporting FHIR applications. Existing NIH programs, including the NHGRI Electronic Medical Records and Genomics Network[118] are already applying FHIR to their clinical studies.

A Workforce to Build a New Computational Community in Biomedicine

ODSS is leading workforce development efforts and bringing disparate research communities together through new training programs. This summer, ODSS matched 21 data-savvy students with computational and technology backgrounds with NIH mentors across 14 institutes, centers, and offices. Student were brought on as Civic Digital Fellows[119] through Coding it Forward, a non-profit focused on developing the next generation of technology leaders or through the Office of Intramural Training and Education's Graduate Data Science Summer Program (GDSSP)[120]. Civic Digital Fellows were placed primarily in administrative or extramural facing offices, while GDSSP fellows spent their summers in intramural research labs. The fellows spent 10 weeks at NIH applying their expertise to challenges in AI and data analysis, improving and automating difficult processes, and developing new algorithms for classification. NIH plans to grow these programs in the future. In spring 2020, NIH, under ODSS leadership, plans to open an announcement for the Data and Technology Advancement (DATA) National Service Sabbatical Scholar Program to recruit a cohort of experienced professionals in computer science or tech-related fields and embed them in high-impact NIH programs for one to two years.

Data Science to Discover New Targets and Therapies

Data science will transform the way researchers approach target discovery, validation, and novel therapeutic identification. NIH programs are leading efforts to advance platforms and tools that

[115] hl7.org/fhir/
[116] grants.nih.gov/grants/guide/notice-files/NOT-OD-19-122.html
[117] grants.nih.gov/grants/guide/notice-files/NOT-OD-19-127.html
[118] genome.gov/Funded-Programs-Projects/Electronic-Medical-Records-and-Genomics-Network-eMERGE
[119] datascience.nih.gov/meet-coding-it-forward-civic-digital-fellows
[120] datascience.nih.gov/meet-graduate-data-science-summer-program-interns

will make these discoveries accessible to researchers and enhance the data science approaches applied to these challenges:

Accelerating Medicines Partnership-Alzheimer's Disease (NIA)
The Accelerating Medicines Partnership-Alzheimer's Disease[121] (AMP-AD) is transforming the way new therapeutic targets and biomarkers are discovered using powerful molecular profiling and advanced information technologies. This public-private partnership also provides an infrastructure for rapid and broad sharing of valuable and robust datasets. The Target Discovery component of the AMP-AD Program applies a systems biology approach to the discovery and validation of new therapeutic targets in an open science research model. Since its inception in 2014, the research teams within the AMP-AD Target Discovery Consortium have established a centralized data resource/infrastructure, the AMP-AD Knowledge Portal[122], for rapid and broad data sharing; generated human data from over 2000 brains and over 1000 plasma samples (across all stages of AD) and made them widely available to researchers; developed network models of disease pathways/targets; and nominated over 100 novel candidate targets. Also, the newly nominated targets and associated data and analyses have been made broadly available through the Agora[123] web-based interactive platform. NIA renewed this ground-breaking program in 2018.

High-Content Screening (HCS) Informatics (NCATS)
At NCATS, automated instrumentation generates high-resolution digital micrographs from many thousands of cellular samples per day, following cell treatment with large pharmaceutical compound libraries. The resulting digital image files that capture cellular phenotypes are produced at a rate of several terabytes per day. Because of the rapidly growing HCS datasets, NCATS has an immediate requirement for expandable data storage and data management systems that are linked with high-speed computer resources for automated image analysis. Investigators are developing a flexible, open-source platform at NCATS to meet these critical needs. The platform is optimized for scalable deployment using both on premise compute resources and cloud-based resources. The plugin-based architecture of the platform allows new customized informatics functions to be added as they are required by individual researchers and is designed to be accessed by both experimental biologists and informaticists.

Platform Technologies
The activities highlighted here enhance and increase access to platform technologies across NIH. Using Other Transaction Authority[124] the STRIDES Initiative is leveraging the commercial cloud

[121] www.nia.nih.gov/research/amp-ad
[122] adknowledgeportal.synapse.org/#/
[123] agora.ampadportal.org/genes
[124] Other Transaction Authority is limited to those government agencies and operational divisions with appropriated authority and is a funding mechanism which targets non-traditional sources and allows a high degree of flexibility Other Transaction Authority is limited to those government agencies and operational divisions with appropriated authority and is a funding mechanism which targets non-traditional sources and allows a high degree of flexibility in how the agreement is awarded. Typical government procurement and grant laws, regulations and policies do not apply to OT awards.

space and will continue to increase access to industry expertise by engaging current partners and additional platform and software analytics partners in the coming year. IAM and the STRIDES Initiative lay a foundation for researchers to search across research datasets on various disease types, minimizing the silo effect created by having unique disease-specific platforms. FHIR will achieve similar goals by implementing standards for clinical research data. NIH workforce development efforts are recruiting experts from computational, mathematical, and related backgrounds and are also opening more opportunities to partner with those communities and engage them in our research. Through workshops on emerging technologies such as artificial intelligence, NIH will continue to engage technical experts and bring them together with the biomedical research community to foster new ideas and adopt emerging technologies. As NIH increases its capacity for platform technologies, a major challenge will be bringing the tools and software needed for usability to the platforms. As part of the strategic plan, NIH has a team working on multi-pronged approaches to address this issue, including potential new funding opportunities and industry partnerships. These and other activities will push NIH and the researchers it supports to continue to leverage advancing platform technologies.

Shaping Current Efforts into Future Results

NIH will continue to build trans-NIH infrastructure to support growing datasets. Ongoing efforts will move NIH toward enhanced abilities to integrate and connect data ecosystems and increase open data sharing and access while maintaining best practices in security and privacy. NIH will build a workforce with computational expertise to work alongside its biomedical experts and ultimately broaden access to data, tools, and resources across diverse scientific communities to advance biomedical and clinical research.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

COMMON FUND (CF)

BUDGET MECHANISM TABLE

(Dollars in Thousands)	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 +/- FY 2020	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	245	$183,110	257	$200,823	284	$221,994	27	$21,171
Administrative Supplements	*(50)*	13,107	*(6)*	1,697	*(3)*	868	*(-3)*	-829
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	145	159,892	136	150,486	122	125,132	-14	-25,354
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	145	$159,892	136	$150,486	122	$125,132	-14	-$25,354
Subtotal, RPGs	390	$356,109	393	$353,006	406	$347,994	13	-$5,012
SBIR/STTR	0	0	0	0	0	0	0	0
Research Project Grants	390	$356,109	393	$353,006	406	$347,994	13	-$5,012
Research Centers:								
Specialized/Comprehensive	33	$38,885	23	$26,785	22	$25,692	-1	-$1,093
Clinical Research	10	19,068	7	13,036	6	10,815	-1	-2,221
Biotechnology	1	772	0	0	0	0	0	0
Comparative Medicine	4	5,721	3	4,159	4	5,804	1	1,645
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	48	$64,445	33	$43,980	32	$42,311	-1	-$1,669
Other Research:								
Research Careers	0	$0	0	$0	0	$0	0	$0
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	118	150,062	151	192,504	132	168,277	-19	-24,227
Other Research	118	$150,062	151	$192,504	132	$168,277	-19	-$24,227
Total Research Grants	556	$570,616	577	$589,490	570	$558,582	-7	-$30,908
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	469	12,711	538	14,884	447	12,350	-91	-2,534
Total Research Training	469	$12,711	538	$14,884	447	$12,350	-91	-$2,534
Research & Develop. Contracts	0	$1,183	0	$577	0	$0	0	-$577
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Intramural Research		15,251		13,129		6,969		-6,160
Res. Management & Support		19,404		21,031		18,566		-2,465
Res. Management & Support (SBIR Admin)		*(0)*		*(0)*		*(0)*		*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	**556**	**$619,166**	**577**	**$639,111**	**570**	**$596,467**	**-7**	**-$42,644**

MAJOR CHANGES IN THE PRESIDENT'S BUDGET REQUEST

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanism and activity detail and these highlights will not sum to the total change for the FY 2021 President's Budget for the Common Fund, which is $42.6 million less than the FY 2020 Enacted level, for a total of $596.5 million. The FY 2021 President's Budget reflects the Administration's fiscal policy goals for the Federal Government. Within that framework, the Common Fund will pursue its highest research priorities through strategic investments and careful stewardship of appropriated funds.

Research Project Grants (-$5.0 million; total $348.0 million): The Common Fund expects to support a total of 406 Research Project Grant (RPG) awards in FY 2021. Estimated awards for FY 2021 include 284 Noncompeting RPGs and 122 Competing RPGs.

Other Research (-$24.2 million; total $168.3 million): The estimated decrease in Common Fund support for the Other Research mechanism reflects planned decreases to activities within several programs. These include decreased support for national service centers in the Transformative High Resolution Cryo-Electron Microscopy program and chemical analysis sites within the Molecular Transducers of Physical Activity program. Additionally, within the Stimulating Peripheral Activity to Relieve Conditions program, there are planned decreases in the anatomical and functional mapping initiative and a technology development initiative, resulting in a reduction in use of Other Transactions Authority.

Intramural Programs (-$6.2 million; total $7.0 million): The estimated decrease in support for Intramural Programs reflects the planned completion of the Common Fund's Regenerative Medicine Program.

BUDGET BY INITIATIVE

(Dollars in Thousands)	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
4D Nucleome	$27,997	$28,860	$27,485
Acute to Chronic Pain Signatures	2,094	16,636	14,648
Big Data to Knowledge (BD2K)	2,605	0	0
Enhancing the Diversity of the NIH-Funded Workforce	52,656	53,713	47,401
Extracellular RNA Communication	6,728	5,846	10,497
Gabriella Miller Kids First Pediatric Research	13,482	13,000	13,000
Genotype-Tissue Expression (GTEx) Resources	772	0	0
Global Health	15,569	11,565	9,261
Glycoscience	19,435	13,362	5,191
Health Care Systems Research Collaboratory	1,988	1,750	1,694
High-Risk, High-Reward Research	206,110	193,100	186,001
NIH Director's Pioneer Award	*45,446*	*54,265*	*51,293*
NIH Director's New Innovator Award Program	*102,692*	*77,815*	*79,795*
Transformative Research Award	*35,149*	*38,402*	*34,659*
NIH Director's Early Independence Award Program	*22,823*	*22,618*	*20,255*
Human BioMolecular Atlas Program (HuBMAP)	15,005	27,031	31,040
Illuminating the Druggable Genome	12,970	13,390	12,971
Knockout Mouse Phenotyping Program	13,757	11,000	0
Library of Integrated Network-Based Cellular Signatures (LINCS)	9,946	87	0
Metabolomics	12,403	12,401	12,000
Molecular Transducers of Physical Activity	44,744	46,126	42,609
New Models of Data Stewardship	199	0	0
NIH Center for Regenerative Medicine (NCRM)	7,597	5,700	0
Protein Capture	1,334	0	0
Science of Behavior Change	12,674	222	0
Somatic Cell Genome Editing	33,324	38,937	44,232
Stimulating Peripheral Activity to Relieve Conditions (SPARC)	51,559	47,268	41,883
Strengthening the Biomedical Research Workforce	56	0	0
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	14,895	51,800	36,290
Undiagnosed Diseases Network	29,207	24,401	21,683
Strategic Planning, Evaluation, and Infrastructure	10,061	22,917	21,129
Subtotal Common Fund	619,166	639,111	579,017
New Initiatives in Common Fund	0	0	17,450
Total Common Fund	**$619,166**	**$639,111**	**$596,467**

JUSTIFICATION OF BUDGET REQUEST

Common Fund

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

Budget Authority (BA):

	FY 2019 Final	FY 2020 Enacted Level	FY 2021 President's Budget	FY 2021 +/- FY 2020
BA	$619,166,000	$639,111,000	$596,467,000	-$42,644,000
FTE	0	0	0	0

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

COMMON FUND NARRATIVE

Overview

The NIH Common Fund (CF) supports research in areas of emerging scientific opportunities, public health challenges, and knowledge gaps that deserve special emphasis; that would benefit from strategic coordination and planning across NIH Institutes and Centers (ICs); and that are designed to achieve specific, high-impact goals and milestones within a 5-10 year timeframe.[125] CF programs aim to change the way science is conducted through the establishment of new scientific fields or paradigms, development of new and innovative technologies, or the generation of data or other resources that catalyze research and enable discovery across the entire spectrum of biomedical research.

Designed as short-term investments with defined goals and deliverables, many CF programs have achieved notable successes during their lifespan that continue to enable biomedical research, including:

- Molecular Libraries and Imaging – Prior to this program, academic researchers did not have access to high-throughput molecular screening facilities that enable the identification of chemical compounds that can be used as research tools and/or that may have novel therapeutic potential. This program established this type of infrastructure within academic institutions and supported screening projects to identify novel compounds with diverse functions.[126] Research from the Molecular Libraries and Imaging program led to the development of a drug currently pending FDA review as a novel treatment for multiple sclerosis. The program also generated many resources that continue to be used by the scientific community, including numerous small molecule

[125] https://commonfund.nih.gov/
[126] https://commonfund.nih.gov/molecularlibraries/index

compounds and probes, several research databases, and PubChem, a widely used web resource for chemical information.[127] Now, five years after CF support for this program ended, the infrastructure that was established continues via support from NIH ICs and from other entities. The program transformed the research enterprise, since it is now relatively straightforward to screen for small molecule probes with specific functions.

- Human Microbiome Project (HMP) – When the HMP began, there was little understanding of the census of microbes that live in and on humans, or how they might contribute to health and disease. HMP transformed our understanding of the human body as an ecosystem including both human and microbial cells by defining the normal human microbiome composition, studying the interplay of microbial and human host biological properties in several diseases/conditions, developing tools and technologies to enable microbiome research, and laying the foundation for an explosion of microbiome research around the globe.[128] This research is informing the development of novel therapies that manipulate the microbial ecosystem and suggests that future probiotic therapies could have powerful and diverse benefits.
- Patient-Reported Outcomes Measurement Information System (PROMIS) – PROMIS created new paradigms for how clinical research information is collected, used, and reported.[129] This program addressed a need in the clinical research community for a rigorously tested tool to measure patient-reported outcomes such as pain, fatigue, physical functioning, emotional distress, and social role participation. The PROMIS tool is now widely used in clinical and research settings.

CF programs often address areas of science that are particularly timely, where breakthrough technologies, public health needs, or scientific challenges create new opportunities for strategic investment. Current examples include:

- The Somatic Cell Genome Editing program is leveraging recent advances in precision genome editing technology to develop broadly useful tools and resources to accelerate the development of new therapies for a variety of genetic diseases.[130]
- The Human BioMolecular Atlas Program (HuBMAP) is capitalizing on recent advances in single cell technology, including advances enabled by the CF's Single Cell Analysis program, to develop a platform to map the human body at single-cell resolution.[131,132]
- Several CF activities are exploring new frontiers in pain research and align with the goals of NIH's Helping to End Addiction Long-term (HEAL) Initiative, a trans-NIH effort to speed scientific solutions to stem the national opioid public health crisis. These activities are supported by the CF, and thus represent an additional NIH commitment beyond HEAL investment to address the opioid public health crisis.
    - The Acute to Chronic Pain Signatures program is developing a set of objective biomarkers to predict if chronic pain is likely to develop after acute pain.[133]

[127] https://pubchem.ncbi.nlm.nih.gov/
[128] https://commonfund.nih.gov/hmp
[129] https://commonfund.nih.gov/promis/index
[130] https://commonfund.nih.gov/editing
[131] https://commonfund.nih.gov/HuBMAP
[132] https://commonfund.nih.gov/Singlecell
[133] https://commonfund.nih.gov/pain

    - An initiative within the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program is generating anatomical and functional datasets from nerve cells that mediate visceral pain.[134]
- Finally, the CF is taking advantage of advances in cloud computing to make CF-supported data resources more useful for the research community through support of a cloud-based data ecosystem.[135] This aligns with the broader NIH efforts to make data Findable, Accessible, Interoperable, and Reusable (FAIR) and increase accessibility of cloud computing. The CF is working closely with the NIH Office of Data Science Strategy to ensure that CF efforts are aligned with and inform broader NIH activities.

Significant efforts are being made to evaluate programs during their lifetime, and outcomes are assessed as programs end. Continuous evaluation during program implementation allows flexibility to modify program management and/or budgets in response to rapidly evolving scientific landscapes, technical challenges, or other unforeseen challenges or opportunities. Funds will be available in FY 2021 for new challenges and opportunities as programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

Overall Budget Policy:
The FY 2021 President's Budget request for the CF is $596.5 million, a decrease of $42.6 million or 6.7 percent compared to the FY 2020 Enacted level. This decrease reflects the planned ramping down of several programs and initiatives and allows support for high-priority activities within existing programs. Several potential new programs are also being considered for an FY 2021 launch: 1) Harnessing Data Science for Health Discovery and Innovation in Africa, 2) Design and Use of Artificial Intelligence Platforms for Biomedical and Behavioral Research, 3) Faculty Institutional Recruitment for Sustainable Transformation (FIRST), and 4) Precision Nutrition.

Description of Activities

The CF supports approximately 30 programs, most of which consist of a series of integrated initiatives that collectively address a set of goals aiming to transform the way research is conducted, the way that health and disease are understood, and/or the way that diseases are diagnosed or treated. Highlighted below are programs that exemplify the science to be supported in FY 2021, and/or which involve significant budget shifts compared to FY 2020.

Several CF programs will receive their last year of support in FY 2020; funds are therefore not requested in FY 2021. These include Knockout Mouse Phenotyping Program,[136] Library of Integrated Network-based Cellular Signatures (LINCS),[137] Regenerative Medicine Program (NIH Center for Regenerative Medicine),[138] and Science of Behavior Change.[139] Information on these programs and their accomplishments can be found on the program websites.

[134] https://commonfund.nih.gov/SPARC
[135] https://commonfund.nih.gov/dataecosystem
[136] https://commonfund.nih.gov/KOMP2
[137] https://commonfund.nih.gov/LINCS
[138] https://commonfund.nih.gov/stemcells
[139] https://commonfund.nih.gov/behaviorchange

Program Portrait: 4D Nucleome

FY 2020 Level: $28.9 million
FY 2021 Level: $27.5 million
Change: -$1.4 million

It is estimated that each human cell contains approximately 2 meters (6.5 feet) of linear DNA, squeezed inside the cell's microscopic nucleus. We know the organization of the nucleus is tightly controlled, and research suggests this organization plays an important role in cell function. However, specific consequences of this organization are not well understood. The 4D Nucleome program is examining how the three-dimensional organization of the nucleus over time (the 4th dimension) affects human health, development, and disease.[140] The first stage of this program has generated a variety of publicly available tools and resources, including nearly 2000 datasets from hundreds of experiments, 52 software packages for data analysis and visualization, and 23 protocols and reagents. Building on the success of the first stage of this program, 4D Nucleome is launching a second stage in FY 2020, aimed at delivering data and tools to the broad biomedical research community to address the role of nuclear organization in health and disease. By enabling research on nuclear organization, the 4D Nucleome program will enhance our understanding of normal cell development and function, and catalyze discovery of new targets for the treatment of human diseases caused by abnormal nuclear organization. Funds requested in FY 2021 will support research on the dynamics and function of genetic material and associated proteins; data integration, modeling, and visualization; transition of research into more biologically relevant cells, tissues, and organisms; an organizational hub; and a data coordination and integration center.

Enhancing the Diversity of the NIH-Funded Workforce

Enhancing the Diversity of the NIH-Funded Workforce, also known as the Diversity Program Consortium (DPC), is a trans-NIH program funded by the CF and managed by the National Institute of General Medical Sciences.[141] Through this national collaborative, NIH works together with institutions and professional societies to advance the DPC's overarching goal of developing, implementing, assessing, and disseminating innovative, effective approaches to research training and mentoring. The DPC consists of several integrated initiatives: Building Infrastructure Leading to Diversity (BUILD), which aims to determine the most effective ways to engage and retain students from diverse backgrounds in biomedical research; National Research Mentoring Network (NRMN), which is developing a national network of mentees and mentors from diverse backgrounds and disciplines; and the Coordination and Evaluation Center (CEC), which coordinates and evaluates DPC activities. Now in its second stage, the DPC is determining the efficacy of the new training and mentoring approaches developed in the first stage of the program. Additionally, two new activities have recently been added to the DPC. One effort aims to establish or enhance Offices of Sponsored Programs at academic institutions to enrich biomedical research and/or research training. The second effort provides an opportunity for institutions who are not currently part of the DPC to employ methods piloted by

[141] https://www.nigms.nih.gov/training/dpc/Pages/default.aspx

the DPC to better understand the effectiveness of these experimental training and mentoring approaches.

Budget Policy:
The FY 2021 President's Budget Request is $47.4 million, a decrease of $6.3 million or 11.8 percent compared to the FY 2020 Enacted level. This level of funding will allow for continued support of the planned DPC efforts in training, mentoring, evaluation, and dissemination.

Extracellular RNA Communication

Ribonucleic acid (RNA) was once thought to exist in a stable form only inside cells, where it plays a key role in translating information coded in genes into proteins that carry out cellular functions. However, we now know that RNA can play additional roles, including roles in cell-to-cell communication via RNAs that are exported from the cell and travel throughout the body. The Extracellular RNA Communication program seeks to understand new paradigms of cellular information exchange based on these extracellular RNAs.[142] Since its founding in 2013, the program has established data standards, a data portal, and tools and reagents available to the scientific community. The program has catalogued extracellular RNA molecules found in human body fluids such as blood plasma, saliva and urine from over 2000 donors. It has also identified potential extracellular RNA biomarkers for nearly 30 diseases, including cardiovascular disease, pregnancy complications, glaucoma, diabetes, and multiple types of cancer. Increased support for this program in FY 2021 will enable development of approaches to rapidly sort complex mixtures of extracellular RNAs associated with various carrier molecules into different populations. It will also enable development of methods to isolate individual members of a specific class of extracellular RNA carriers called extracellular vesicles. The ability to isolate and sort different types of RNAs and associated carriers will allow researchers to investigate their distinct roles in human health and disease and may also ultimately lead to the development of a novel class of therapies that use RNA to alter cell function.

Budget Policy:
The FY 2021 President's Budget Request is $10.5 million, an increase of $4.7 million or 79.6 percent compared to the FY 2020 Enacted level. This increase will enable development of novel approaches to better sort and isolate specific types of extracellular RNAs and their carriers, allowing researchers to decipher the specific roles that different extracellular RNAs may play in health and disease.

Gabriella Miller Kids First Pediatric Research Program

The Gabriella Miller Kids First Pediatric Research program (Kids First) aims to catalyze pediatric research by making large amounts of high-quality genetic and clinical data from pediatric patient cohorts widely available and easy to use for the entire biomedical research community.[143] The Kids First program supports a data resource that integrates data from patients with childhood cancer or structural birth defects. Researchers analyze these data to understand how genetic mutations lead to birth defects or to cancer, and to discover whether there are shared

[142] https://commonfund.nih.gov/exrna
[143] https://commonfund.nih.gov/KidsFirst

contributions to both conditions. There is considerable scientific evidence that examining childhood cancer and structural birth defects data together will uncover new connections between them that would not have been discovered if they were examined independently. Having these data sets together in a single, widely accessible resource is anticipated to facilitate new discoveries and novel ways of thinking about these conditions. To date, the program has sequenced more than 20,000 samples from childhood cancer and structural birth defects cohorts, and clinical and genetic sequence data from 9 datasets are publicly available. Because investigators funded through this program are dedicated to translating the knowledge gained from these data sets to new therapeutic approaches as quickly as possible, end-user support is an important focus. Funds requested in FY 2021 from the Pediatric Research Initiative Fund will be used to support pediatric research, consistent with the Gabriella Miller Kids First Research Act, and remain constant at statutory level set by this legislation. Requested funds will be used to continue support for the Kids First Data Resource, genetic sequencing of patient cohorts, and research projects to demonstrate the value of the Kids First data to the broader research community.

Budget Policy:
The FY 2021 President's Budget Request is $13.0 million, unchanged from the FY 2020 Enacted level. Programmatic funding from the Pediatric Research Initiative Fund remains constant at the $12.6 million statutory level. The remainder of the funds are requested in the regular CF appropriation to support research management activities.

Glycoscience

The Glycoscience program aims to create new resources, tools, and methods to make the study of glycans (sugars) more accessible to the biomedical research community.[144] Glycans are present on a number of biologically important molecules and play critical roles in a wide range of activities, including fighting viruses and bacteria, movement of proteins within cells to carry out important functions, and growth of neurons. However, due to their complex nature, the study of glycans has been largely inaccessible to many researchers. Important contributions of the Glycoscience program to date include development of techniques for identifying glycans that are especially difficult to study, probes to study glycans in bacterial cell walls, standards for glycan chemical synthesis, methods for high-throughput glycan studies, and glycoscience educational materials. The Glycoscience program, having developed valuable tools, methods, and resources to facilitate the study of glycans across a wide range of scientific fields, winds down activities in FY 2021.

Budget Policy:
The FY 2021 President's Budget Request is $5.2 million, a decrease of $8.2 million or 61.2 percent compared to the FY 2020 Enacted level. This decrease in support reflects the planned ramping down of the program in FY 2021.

[144] https://commonfund.nih.gov/Glycoscience

High-Risk, High-Reward Research Program

The High-Risk, High-Reward Research (HRHR) program supports exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH mission through four complementary initiatives: the Pioneer Award, New Innovator Award, Transformative Research Award, and Early Independence Award.[145] These awards are intended to support transformative science that is inherently difficult and risky, but necessary to accelerate the pace of scientific discovery and advance human health. Independent evaluations found that Pioneer and New Innovator awardees produce more innovative, risky, and impactful research compared to typical R01 awards. Additionally, the HRHR program has served as the model for many other high-risk, high-reward awards across NIH ICs, demonstrating trans-NIH commitment to fostering innovation and risk-taking in pursuit of transformative discoveries. The HRHR program has supported numerous fundamental discoveries and the development of novel tools that are now demonstrating wide-spread impact. Examples include:

- Expansion microscopy – Developed by Pioneer Awardee Dr. Edward Boyden, expansion microscopy is a groundbreaking technique that allows researchers to expand biological samples up to 100-fold.[146] This allows visualization of cells and tissues on a scale that surpasses the limits of conventional light microscopy, enabling exploration of cellular structures and biological molecules that otherwise would not be possible. This technique has been used to explore a wide range of research questions because of its applicability in numerous biological models that range from bacteria to human brain tissue.
- Novel antibiotics – Addressing the growing public health crisis of antibiotic-resistant bacteria, research by Transformative Research Awardee Kim Lewis led to the discovery of teixobactin, a novel antibiotic effective against a wide variety of bacteria including those with resistance to other antibiotics. Since publication, this discovery has generated over 1400 citations, providing an entirely novel option in the fight against antibiotic-resistant bacteria.

Funds requested in FY 2021 will be used to support additional high-risk projects with the potential for extraordinary impact.

Budget Policy:

The FY 2021 President's Budget Request is $186.0 million, a decrease of $7.1 million or 3.7 percent compared to the FY 2020 Enacted level. This level of support will allow NIH to continue to invest in high-risk research projects with the potential to achieve remarkable scientific breakthroughs and advance human health.

Human BioMolecular Atlas Program

The Human BioMolecular Atlas Program (HuBMAP) aims to catalyze development of an open, global framework for comprehensively mapping the human body at the level of individual cells.[147] Understanding the specialization, spatial organization, and interaction of cells is critical to fully comprehending the health and function of all our organs and tissues. HuBMAP will map

[145] https://commonfund.nih.gov/highrisk
[146] https://www.ncbi.nlm.nih.gov/pubmed/?term=25592419
[147] https://commonfund.nih.gov/HuBMAP

a small percentage of the human body (tens of millions of cells out of the trillions in the human body), but it will work with the broader community to establish tools, infrastructure, and standards with the expectation that the research community will continue to build upon these maps in the future. As this data resource grows over time, it will result in a complete human body map at the cellular level, ultimately contributing to a resource like Google Maps for the human body. If successful, these maps will enable and encourage future studies and new insights into individual variation and tissue changes across the lifespan and health/disease continuum. This program is expected to leverage close partnership with companies and international agencies so that multiple funding sources are applied to this global challenge. HuBMAP continues to grow in FY 2021, using requested funds to continue efforts in tissue mapping and technology development, while increasing support for data coordination and launching a new initiative to support data analysis.

Budget Policy:
The FY 2021 President's Budget Request is $31.0 million, an increase of $4.0 million or 14.8 percent compared to the FY 2020 Enacted level. The increased level of support will allow continuation of several HuBMAP activities while supporting increased data coordination and new efforts in data analysis.

Somatic Cell Genome Editing

Recent developments in genome editing techniques are allowing researchers to precisely change specific sequences in the human genome. These advances raise the possibility of a fundamentally new approach to treat genetic disorders, including common diseases such as cancer and diabetes, as well as rare conditions such as Duchenne muscular dystrophy, Huntington's disease, and cystic fibrosis. The Somatic Cell Genome Editing program aims to develop quality tools to perform safe and effective genome editing in human patients, ultimately reducing the time and cost to develop new therapies for diseases caused by changes to the genetic code.[148] These tools will need to function specifically on the disease gene to minimize unintended consequences. They will also need to be delivered selectively to the cells within the body that are affected by the disease, avoiding unaffected cells and reproductive cells so that changes are not passed on to future generations. In FY 2021, requested funds will be used for increased support to develop improved and validated gene delivery systems capable of targeting specific cells and tissues safely and effectively. Support will also continue for efforts to develop an expanded set of gene editing technologies, better animal models, approaches to assess unintended biological effects, and a coordination and dissemination center.

Budget Policy:
The FY 2021 President's Budget Request is $44.2 million, an increase of $5.3 million or 13.6 percent compared to the FY 2020 Enacted level. This increase in support will allow development and refinement of a comprehensive suite of resources to speed the translation of gene editing approaches into the clinic.

Stimulating Peripheral Activity to Relieve Conditions

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

The Stimulating Peripheral Activity to Relieve Conditions (SPARC) program aims to accelerate development of therapeutic devices that modulate electrical activity in nerves to improve organ function.[149] Therapeutic manipulation of nerve function could be a novel approach to treat diverse diseases and conditions, such as hypertension, heart failure, gastrointestinal disorders, type 2 diabetes, and more. However, there is an urgent need to better understand the precise pattern of end-organ neural circuitry, so that the correct nerves can be targeted and the most beneficial amounts and types of stimulation can be applied. SPARC is a high risk, goal-driven basic research endeavor to develop foundational knowledge and technologies for an entirely new class of neuromodulation devices. SPARC supports interdisciplinary teams of investigators to develop neural circuit maps and models, along with technologies to measure and manipulate nerve-organ interactions. Through partnerships with industry and physicians, the program supports human clinical studies that will serve to validate or refine neural circuit maps built from animal data. The mapping data, models, technologies, and protocols generated will be publicly available through an online resource to share tools and advancements. This program uses Other Transaction Authority for selected initiatives, which allows high levels of flexibility, responsiveness to adjust program components, and ability to engage with non-traditional partners as needed to address specific, high-risk goals within this complex, interdisciplinary, and rapidly evolving area of science.

Budget Policy:
The FY 2021 President's Budget Request is $41.9 million, a decrease of $5.4 million or 11.4 percent compared to the FY 2020 Enacted level. This level of support reflects a planned decrease in mapping efforts and tool development, while maintaining support for data coordination, partnerships to pursue clinical studies, and studies on neural circuity mediating visceral pain.

Transformative High Resolution Cryo-Electron Microscopy

Knowing the structure of a biological molecule reveals important information about how it functions and can provide insight into potential drug targets for fighting disease. However, techniques commonly used to investigate molecular structure often use harsh chemicals or treatments that can change the structure, producing inaccurate or incomplete results. Cryo-electron microscopy enables researchers to determine the structures of a wide range of biological molecules with greater accuracy, which helps identify new therapeutic targets for vaccines and drugs. However, the high cost of cryo-electron microscopes means that access to this technology is out of reach for many scientists. The Transformative High Resolution Cryo-Electron Microscopy program (CryoEM) aims to broaden access to cryo-electron microscopy for biomedical researchers through support of national service centers, improvement of technology, and training.[150] In FY 2021, the requested budget will support efforts to increase access to cryo-electron tomography, a related technology that enables improved imaging of molecules within intact cells and tissues in three dimensions, as well as continued support for CryoEM service centers and training.
Budget Policy:

[149] https://commonfund.nih.gov/sparc
[150] https://commonfund.nih.gov/CryoEM

The FY 2021 President's Budget Request is $36.3 million, a decrease of $15.5 million or 29.9 percent compared to the FY 2020 Enacted level. This level of support reflects a planned decrease in funding for cryo-electron microscopy national service centers, while maintaining support for broadening access to state-of-the-art technologies in cryo-electron tomography.

Strategic Planning, Evaluation, and Infrastructure

Management of the CF requires that certain activities be undertaken for the benefit of the CF as a whole. Strategic planning and evaluation, described below, have been long-standing costs. However, as data-intensive strategies are increasingly undertaken to achieve the goals of CF programs, infrastructure to address challenges facing all data management centers has become necessary. This infrastructure, referred to as the Common Fund Data Ecosystem, will help to ensure that all CF data sets are FAIR, provide training for users to operate on the data in a cloud environment, and ensure that CF data continue to be available after individual programs are completed. This Data Ecosystem will amplify the impact of several CF programs by enabling researchers to interrogate multiple disparate data sets, and thereby make new kinds of scientific discoveries that were not possible before.

Strategic planning is undertaken every year to identify new scientific challenges and opportunities. CF strategic planning encompasses both the identification of broadly relevant scientific challenges and opportunities for strategic investments (Phase 1 planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic (Phase 2 planning). Phase 1 strategic planning often involves gathering broad input from stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase 2 strategic planning often involves specific consultations with external experts, analysis of NIH and worldwide research portfolios, and literature reviews to articulate specific gaps and areas of research where opportunities for transformative progress are possible.

Since CF programs are goal-driven, evaluation is critical to monitoring progress and developing strategies to adapt program management. Evaluation includes both formal and informal evaluative activities. Informal evaluation involves convening grantees and NIH-wide teams to review progress, discuss new challenges, and develop strategies to adapt as part of routine program management. It also involves gathering input from external consultants and using their input, together with internal analysis, to help guide the implementation of the program. Formal evaluations involve the development of baseline data for new programs and the development of multiple metrics of outcomes. The utility of data, resources, technologies, and other program outputs is assessed through surveys, expert opinion, and the analysis of bibliometric data such as citation analyses.

Funds Available for New Initiatives

Planning for potential new FY 2021 programs involved discussions with NIH Leadership, NIH IC Directors, and editors from diverse and well-respected scientific journals, who have a broad view of the scientific landscape. From these discussions, several promising ideas emerged, and selected concepts are currently undergoing planning for a potential launch in FY 2021 (pending

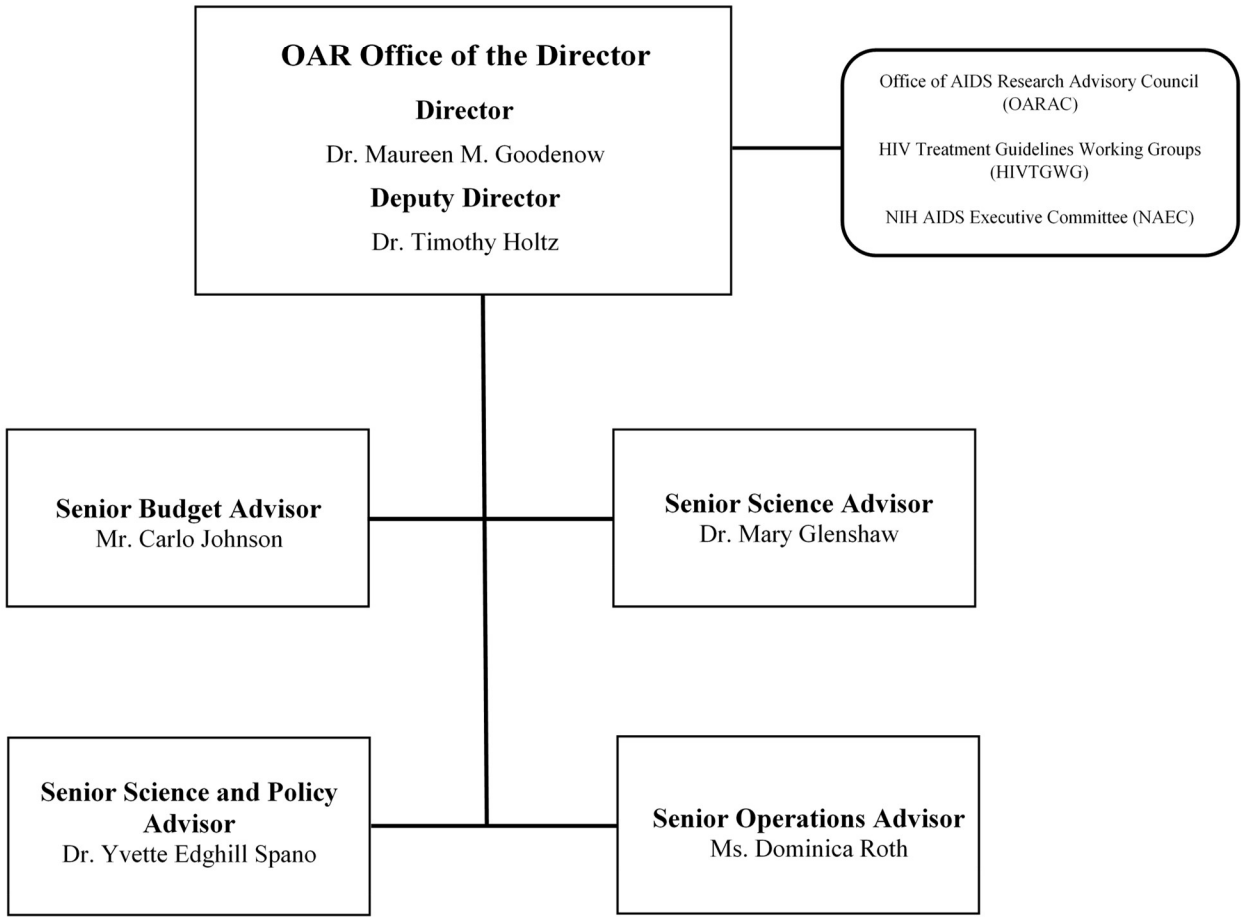
availability of funds). One potential new program, Harnessing Data Science for Health Discovery and Innovation in Africa, would explore whether advances in data science applied in the African context can spur new health discoveries and catalyze innovation in healthcare and health research on the continent. A second program, Design and Use of Artificial Intelligence Platforms for Biomedical and Behavioral Research, would implement catalytic, time-limited initiatives in response to recommendations from the NIH Advisory Committee to the Director. This program would support strategic investments to generate broadly useful data sets in a way that will be amenable to artificial intelligence approaches; it will also catalyze formation of "bilingual" teams that bring health research expertise and artificial intelligence expertise together for high priority research questions. Third, the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program would aim to create cultures of inclusive excellence at NIH-funded institutions, establishing and maintaining scientific environments that can cultivate and benefit from a full range of talent. This potential program would establish a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address bias, faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts. Finally, a potential program in Precision Nutrition would aim to understand individual responses to diet, enabling tailored dietary recommendations to be provided by physicians as well as development of tools to allow individuals to make more informed decisions about healthy food choices. The focus and scope of these potential programs may change as additional planning activities are conducted.

NIH HIV/AIDS RESEARCH BUDGET

NOTE: Program discussion and amounts do not include HIV/AIDS activities of the Agency for Healthcare Research and Quality, which is proposed for consolidation into NIH in FY 2021 as the National Institute for Research on Safety and Quality (NIRSQ).

ORGANIZATION CHART

NATIONAL INSTITUTES OF HEALTH
OFFICE OF AIDS RESEARCH



BUDGET AUTHORITY BY INSTITUTE AND CENTER

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

Institute, Center, and Office	FY 2019 Final [1]	FY 2020 Enacted Level [2]	FY 2021 President's Budget	FY 2021 +/- FY 2020
NCI	$241,979	$241,975	$220,132	-$21,843
NHLBI	83,715	84,715	77,068	-7,647
NIDCR	18,734	18,984	17,270	-1,714
NIDDK	33,203	34,135	31,054	-3,081
NINDS	39,192	41,082	37,374	-3,708
NIAID	1,743,221	1,779,113	1,632,583	-146,530
NIGMS	8,300	-	-	-
NICHD	144,367	144,895	131,815	-13,080
NEI	1,153	388	353	-35
NIEHS	5,342	5,342	4,860	-482
NIA	20,426	22,622	20,580	-2,042
NIAMS	4,571	4,587	4,173	-414
NIDCD	2,128	2,128	1,936	-192
NIMH	178,899	183,991	167,382	-16,609
NIDA	264,814	261,140	237,567	-23,573
NIAAA	30,556	31,879	29,001	-2,878
NINR	13,100	16,350	14,874	-1,476
NHGRI	5,533	3,302	3,538	236
NIBIB	839	1,839	1,673	-166
NIMHD	22,701	22,780	20,724	-2,056
NCCIH	611	748	680	-68
FIC	24,239	24,389	22,187	-2,202
NLM	9,322	9,322	8,480	-842
OD				
OAR	62,256	62,256	56,636	-5,620
ORIP	78,099	78,099	71,049	-7,050
Subtotal, OD	140,355	140,355	127,685	-12,670
TOTAL, NIH	**$3,037,300**	**$3,076,061**	**$2,812,989**	**-$263,072**

[1] Reflects effects of Secretary's transfer
[2] Includes effects of FY 2020 HIV/AIDS transfers

BUDGET AUTHORITY BY MECHANISM

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS [1]
(Dollars in Thousands)

MECHANISM	FY 2019 Final [2]		FY 2020 Enacted Level		FY 2021 President's Budget		FY 2021 +/- FY 2020	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,520	$1,404,709	1,458	$1,361,479	1,341	$955,066	-117	-$406,413
Administrative Supplements	*(60)*	24,263	*(38)*	10,347	*(25)*	7,336	*-13*	-3,011
Competing	452	330,860	518	383,342	540	633,483	22	250,141
Subtotal, RPGs	1,972	$1,759,832	1,976	$1,755,168	1,881	$1,595,885	-95	-$159,283
SBIR/STTR	30	17,361	29	18,601	28	17,013	-1	-1,588
Research Project Grants	2,002	$1,777,193	2,005	$1,773,769	1,909	$1,612,898	-96	-$160,871
Research Centers:								
Specialized/Comprehensive	57	$116,811	58	$130,828	58	$124,009	0	-$6,819
Clinical Research	0	0	2	986	2	986	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	18	69,990	20	71,361	18	64,939	-2	-6,422
Research Centers in Minority Institutions	0	96	0	1,270	0	1,143	0	-127
Research Centers	75	$186,897	80	$204,445	78	$191,077	-2	-$13,368
Other Research:								
Research Careers	253	$44,514	260	$45,118	248	$41,880	-12	-$3,238
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	5,149	0	5,150	0	4,790	0	-360
Biomedical Research Support	31	2,249	31	1,600	29	1,456	-2	-144
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	128	56,096	121	52,799	110	48,083	-11	-4,716
Other Research	412	$108,008	412	$104,667	387	$96,209	-25	-$8,458
Total Research Grants	2,489	$2,072,098	2,497	$2,082,881	2,374	$1,900,184	-123	-$182,697
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	77	$3,284	81	$3,227	81	$3,136	0	-$91
Institutional Awards	258	14,904	257	15,020	251	14,374	-6	-646
Total Research Training	335	$18,188	338	$18,247	332	$17,510	-6	-$737
Research & Develop. Contracts	88	$363,884	76	$387,439	76	$340,731	0	-$46,708
(SBIR/STTR) (non-add)	*(10)*	*(7,792)*	*(9)*	*(10,105)*	*(9)*	*(9,285)*	*0*	*-820*
Intramural Research		$359,724		$356,814		$336,695		-$20,119
Res. Management and Support		161,150		168,424		161,233		-7,191
Res. Management & Support (SBIR Admin) (non-add)								
Office of the Director - Appropriation [3]		*140,355*		*140,355*		*127,685*		*-12,670*
Office of the Director - Other		62,256		62,256		56,636		-5,620
ORIP (non-add) [3]		*78,099*		*78,099*		*71,049*		*-7,050*
Total, NIH Discretionary B.A.		**$3,037,300**		**$3,076,061**		**$2,812,989**		**-263,072**

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

[2] Reflects effects of Secretary's transfer

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

BUDGET AUTHORITY BY ACTIVITY

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

Overarching Priorities	FY 2017 Actual	FY 2018 Actual [1]	FY 2019 Final [1]	FY 2020 Enacted Level	FY 2021 President's Budget	FY 2021 +/- FY 2020
Reduce the Incidence of HIV	$687,495	$714,553	$741,401	$737,348	$660,231	-$77,117
Develop Next-Generation HIV Therapies	362,820	364,484	368,912	365,526	313,066	-$52,460
Research Toward a Cure for HIV[2]	170,375	175,757	187,777	197,637	180,794	-$16,843
Address HIV-Associated Comorbidities, Coinfections, and Complications	556,608	517,884	531,440	543,531	501,591	-$41,940
Cross-Cutting Areas	1,222,763	1,222,703	1,207,770	1,232,019	1,157,307	-$74,712
Total	**$3,000,061**	**$2,995,381**	**$3,037,300**	**$3,076,061**	**$2,812,989**	**-$263,072**

[1] Reflects effects of Secretary's transfer

[2] Beginning in FY 2017, Research Toward a Cure for HIV/AIDS became a separate activity. Dollars for Research Toward a Cure for HIV/AIDS were previously included within other science areas, such as Next Generation Therapies, Crosscutting--Basic Research, and Reducing Incidence of HIV/AIDS.

JUSTIFICATION OF BUDGET REQUEST

Office of AIDS Research
NIH AIDS Research Budget Justification

Budget Authority (BA):

FY 2019 Final	FY 2020 Enacted Level	FY 2021 President's Budget	FY 2021+/- FY 2020
$3,037,300,000	$3,076,061,000	$2,812,989,000	-$263,072,000

NIH, Office of the Director, Office of AIDS Research (OAR)

Mission Statement

To ensure NIH HIV research funding aligns with high-priority research areas and to facilitate the maximum return on investment.

DIRECTOR'S OVERVIEW/PROGRAM NARRATIVES

Director's Overview

NIH's investments in Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) research have, over more than three decades, produced groundbreaking advances in understanding the basic virology, immunology, and pathogenesis of HIV. Research discoveries enabled the development of safe, effective antiretroviral medications that can extend the lifespan of people with HIV and the design and implementation of effective strategies to prevent HIV transmission and acquisition. Nonetheless, globally including the United States, new infections continue at alarming rates in some locations while remaining unchanged in others, reflecting inequalities by race, ethnicity, sex, gender, age, socioeconomic status, and geography. NIH will continue to lead basic, clinical, behavioral, and translational research to develop cutting-edge solutions to address the ongoing challenges of the HIV pandemic.

There is little doubt that the HIV pandemic will continue to affect virtually every nation in the world well into the next century. It is important to broaden our understanding of the affected populations to more effectively tailor prevention and treatment strategies. To accomplish these objectives, a major advance in moving NIH's research efforts forward is the 21st Century Cures Act, passed in 2016. This act amends the Public Health Service Act to charge researchers with gathering inclusive clinical research data to improve the health of women, members of minority groups, and relevant age categories. Individuals from minority groups – including racial and ethnic minorities and sexual and gender minorities – historically have been underrepresented in biomedical research. NIH has implemented efforts to address inclusion and exclusion of

pediatric and older adult populations relating to research studies, which will increase the knowledge of how to improve and support health across the lifespan.

To provide leadership in setting the national and global HIV research agenda, the NIH Office of AIDS Research (OAR) was established in 1988 through Section 2353 of the Public Health Service Act. Located within the NIH Office of the Director, Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), OAR is authorized to:

- Oversee, coordinate, and manage all NIH HIV-related research;
- Establish research priorities;
- Develop the strategic plan for HIV research;
- Ensure that funds are invested in the areas of highest scientific priority; and
- Address emerging opportunities.

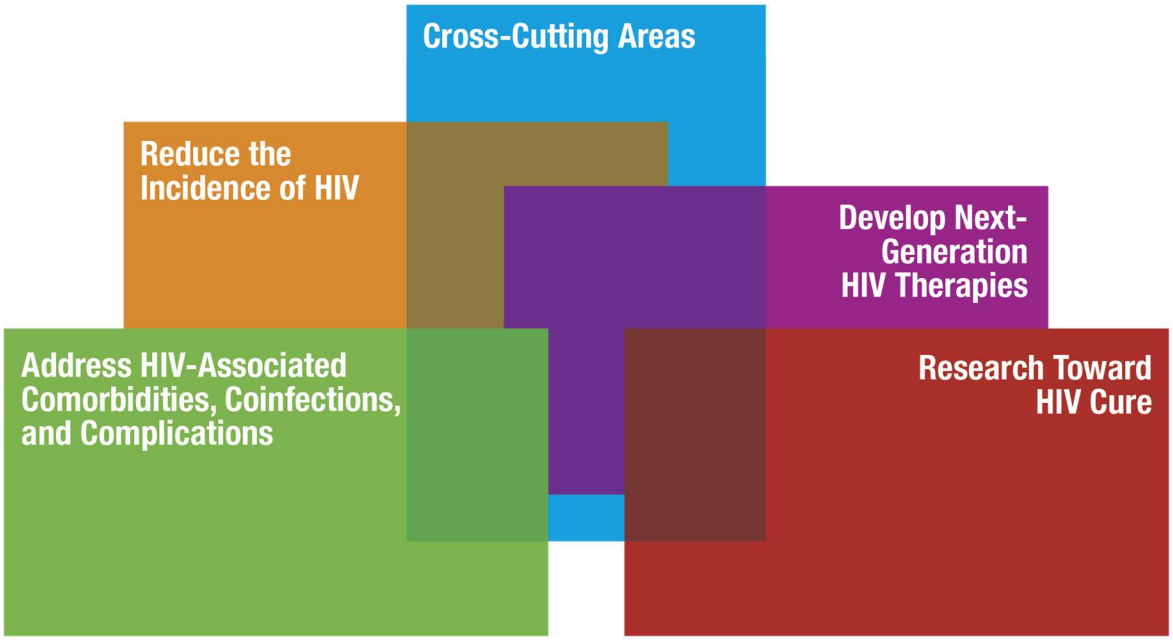
Coordination & Management: OAR coordinates the scientific, budgetary, legislative, and policy components of the NIH HIV/AIDS research program by leading the NIH-wide HIV research strategic planning, priority-setting, and resource allocation to:

- Promote, coordinate, and implement cost-sharing between Institutions, Centers, and Offices (ICOs) and OAR;
- Accelerate discovery, enhance collaboration, and minimize duplication; and
- Translate basic research discoveries into clinical practice and public health implementation.

Priority-setting: OAR partners with stakeholders across the NIH, governmental agencies, research organizations, and communities to establish HIV research priorities (Figure 1) in the global fight against HIV to:

- Reduce the incidence of new HIV infections;
- Develop next-generation HIV therapies;
- Research toward HIV Cure;
- Address HIV-associated comorbidities, coinfections, and complications (CCCs); and
- Support a broad array of cross-cutting research areas to combat the HIV pandemic.

Figure 1. NIH HIV Research Priorities



Reduce the Incidence of HIV
- Vaccines
- Pre-exposure Prophylaxis
- Microbicides and MPTs
- HIV Testing
- Treatment as Prevention
- Monoclonal Antibodies

Address HIV-Associated Comorbidities, Coinfections, and Complications
- Coinfections
- Neurologic Complications
- Malignancies
- Cardiovascular Complications
- Mental Illness and Substance Use
- Metabolic Disorders
- Across the Lifespan

Cross-Cutting Areas
- Basic Virology and Immunology
- Behavioral and Social Sciences
- Epidemiology
- Health Disparities
- Information Dissemination
- Implementation Science
- Research Training, Infrastructure, and Capacity Building

Develop Next-Generation HIV Therapies
- Less Toxic, Longer Lasting ART
- Novel HIV Targets & Inhibitors
- Novel Immune-Based Therapies
- Engagement, Adherence, and Retention in Care
- Self-Testing Technologies
- U = U

Research Toward HIV Cure
- Sustained ART-free Viral Remission
- Viral Eradication
- Viral Latency and Sanctuaries
- Cure Ethics and Acceptability

Strategic Planning: OAR develops the *NIH Strategic Plan for HIV and HIV-Related Research* (The Plan),[151] which identifies research priorities for NIH-funded intramural and extramural research. The Plan informs the general public, scientific community, Congress and policy-makers, and communities impacted by HIV about the NIH HIV research agenda. NIH is transitioning from annual or biennial Plans to a five-year strategic plan for FY 2021 to 2025 to encompass a longer-term vision for the research agenda.

The five-year Plan outlines an integrated approach for the NIH HIV/AIDS research program that leverages partnerships to develop new and innovative strategic research efforts to effectively end the HIV pandemic and improve health outcomes of all persons with or at risk for HIV. The strategic goals of the Plan closely align with the goals of the current *National HIV/AIDS Strategy for the United States: Updated to 2020* (NHAS)[152] and the National Viral Hepatitis Action Plan (NVHAP) 2017-2020.[153]

[151] www.oar.nih.gov/hiv-policy-and-research/strategic-plan
[152] www.hiv.gov/federal-response/national-hiv-aids-strategy/nhas-update
[153] www.hhs.gov/sites/default/files/National%20Viral%20Hepatitis%20Action%20Plan%202017-2020.pdf

The Plan provides a framework for NIH efforts in support of the *Ending the HIV Epidemic: A Plan for America* (EHE) – a once-in-a-generation opportunity to eliminate new HIV infections in our nation. EHE is working to reduce new infections by 75 percent in the next 5 years and by 90 percent in the next 10 years, averting more than 250,000 new HIV infections in that span.[154]

Budgeting: OAR continues to manage the allocation of NIH HIV research funds to the ICOs to advance HIV science and ensure that funds are aligned with the highest research priorities. Based on the Plan and priorities, OAR evaluates the NIH-wide research portfolio and, in consultation with the ICOs, allocates resources to addresses emerging research opportunities.

Stakeholder Engagement: OAR convenes stakeholders, encourages collaboration, and catalyzes innovation to address emerging scientific and public health challenges. To ensure that the NIH HIV research agenda addresses the most important scientific questions associated with the pressing needs of HIV-affected communities over the next five years, OAR is conducting a series of Listening Sessions across the country to gather input from scientists, advocates, health care providers, public health implementers, community representatives, and other stakeholders. These sessions provide a platform for the OAR Director and staff to hear stakeholder perspectives on key scientific questions, research methodologies, and capacity issues of local and regional importance. Outcomes from the sessions will inform OAR planning and budgeting recommendations to the NIH Director.

Program Descriptions, Accomplishments, and Future Directions

The following selected programs and activities focus on the highest HIV research priorities to illustrate the NIH Director's theme of *Science with an Eye to the Future: The Long Arc of Research.*

The research response to the HIV/AIDS pandemic has had an impactful and transformative arc on biomedical research spanning more than three decades (Table 1). From identification of the first cases of AIDS and delineation of HIV as the causative agent in the early 1980s to the groundbreaking initiative to end the HIV epidemic in the United States by 2030 through enhancing implementation of effective evidence-based prevention and care strategies in the hardest-hit jurisdictions, HIV research at NIH produces life-saving changes for people with HIV (PWH), catalyzes paradigm-changing approaches to research infrastructure, methodologies, and strategies that extend across research fields, and raises the future feasibility of an HIV vaccine and a cure.

[154] www.hhs.gov/sites/default/files/ending-the-hiv-epidemic-fact-sheet.pdf

Table 1. Highlights of discovery from NIH HIV/AIDS supported research from 1981–2019.

Year	Event
1981	CDC published the first *Morbidity and Mortality Weekly Report* (MMWR) about a disease later named the Acquired Immune Deficiency Syndrome (AIDS).
1982	The National Institutes of Health (NIH) provided the first HIV/AIDS funding.
1983	Congress passed the first bill with funding for AIDS research and treatment. The NIH and the Pasteur Institute announced the viral causative agent.
1985–1987	NIH researchers discovered that zidovudine (ZDV); also known as azidothymidine (AZT) suppressed viral replication becoming the first antiretroviral approved by the FDA.
1988	Congress established the Office of AIDS Research (OAR) to coordinate HIV/AIDS research across NIH.
1996–1997	Combining antiretroviral drugs led to the development of highly active antiretroviral therapy (HAART), which became the new standard of HIV care. NIH funded PACTG 076 clinical trial showed ZDV treatment of pregnant women with HIV and their infants reduced perinatal infection by 67 percent.
1998	The CDC issued the first national treatment guidelines for the use of antiretroviral therapy in adults and adolescents with HIV.
2003	President Bush established the U.S. President's Emergency Plan for AIDS (PEPFAR) to provide antiretroviral therapy (ART) to resource-limited countries.
2006	A new fixed-dose combination of three widely used antiretroviral drugs is developed that can be taken in a single tablet once a day, alone or in combination with other antiretroviral products for treatment in adults.
2013	The FDA approved a second-generation integrase inhibitor dolutegravir that could be widely used by PWH.
2016–2017	The U=U slogan was launched by the Prevention Access Campaign. The CDC officially backed the science behind the campaign and was endorsed by HIV organizations around the world.
2019	*Ending the HIV Epidemic: A Plan for America* is announced, with the goal of reducing the number of new HIV infections in the United States by 75 percent within five years, and then by at least 90 percent within 10 years.

Overall Budget Policy: The FY 2021 President's Budget request for the NIH-wide HIV/AIDS research agenda is $2,813.0 million, a decrease of $263.1 million or 8.6 percent compared to the FY 2020 Enacted Level. The FY 2021 budget request reflects the ambitious but achievable goal to end the HIV epidemic in the United States by 2030, as well as achieve HIV pandemic control globally. NIH HIV research investments focus on the expansion of innovative basic science discoveries in virology, human immunology, and biotechnology to accelerate HIV vaccine efforts through the research pipeline from basic discovery and preclinical studies to the impending outcomes from landmark clinical trials in diverse settings around the world. The NIH HIV research portfolio includes innovative interventions and new implementation strategies for pre-exposure prophylaxis to significantly reduce the number of new HIV infections, and new

long-acting therapies to improve viral load suppression among people with HIV to levels that prevent transmission. Novel technologies will expand point-of-care and self-testing modalities for monitoring HIV viral load suppression, while gene therapy strategies are in development for delivery of an HIV cure. The FY 2021 President's Budget request supports research to address the health and quality of life of persons with HIV, including comorbidities, co-infections, and complications resulting from the near-normal lifespan now afforded by simplified, potent antiretroviral therapies. The health effects of HIV infection and treatment often intersect social health determinants, including racial, ethnic, gender, geographic disparities, poverty, stigma, and socioeconomic disenfranchisement. NIH HIV research strategies employ approaches that include high quality, multidisciplinary, community-engaged research and implementation science to best understand the most effective interventions. Training and building capacity of new and early stage investigators is an enhanced priority to build the skills and scope of current and future generations of HIV researchers who can address 21st century challenges with 21st century solutions.

Reduce the incidence of HIV

Developing an effective preventive vaccine against HIV remains a critical research goal. In 2009 a key milestone was reached with results from the RV144 vaccine trial, supported by the Department of Defense, NIH, and the government of Thailand, which showed partial efficacy (31 percent) in a large-scale field trial of an experimental vaccine regimen.[155] NIH is currently supporting additional large-scale efficacy trials of candidate HIV vaccine regimens with new products developed since RV144. In January 2020, vaccine administration was discontinued in the HVTN 702 trial, led by the Pox-Protein-Public-Private Partnership (P5), as results indicated that the regimen did not prevent HIV, although there were no safety concerns for study participants.[156,157] Two other HIV vaccine trials using different vaccines, HVTN705/HPX2008 (Imbokodo) and HPX3002/HVTN 706 (Mosaico), are ongoing in multiple international sites with initial results anticipated in 2021. In addition, a robust pipeline of candidate vaccine products includes multiple clinical studies in various stages of testing in humans.

Basic, clinical, and translational research to evaluate the human immune response to vaccine remains a critical priority. Advances in imaging technologies have led to the development of vaccine candidates that more closely mimic HIV envelope structural components and could provide the foundation for improved vaccines to induce protective immunity. In preparation for an increased number of vaccine efficacy clinical trials, NIH has strategically invested in expanding vaccine product manufacturing capabilities to meet future research demands. The Division of AIDS, Vaccine Research Program, Translational Research Branch, in the National Institute of Allergy and Infectious Disease, works closely with academic institutions, biotech, pharmaceutical companies, non-profit organizations, vaccine trial networks, contract manufacturing and contract research organizations to advance clinical HIV vaccine development.[158]

[155] www.hivresearch.org/rv144-trial
[156] www.niaid.nih.gov/diseases-conditions/empirical-approach
[157] www.nih.gov/news-events/news-releases/experimental-hiv-vaccine-regimen-ineffective-preventing-hiv
[158] www.niaid.nih.gov/research/daids-translational-research-program

In parallel with vaccine-based prevention strategies, antibody-mediated protection (AMP) studies are testing biologicals as alternatives for prevention in uninfected individuals. Studies in multiple countries are in progress to determine whether or not periodic infusions or injections of certain broadly neutralizing antibodies (bNAbs) can prevent HIV acquisition in different populations of at-risk individuals. While the studies represent significant advances toward prevention of HIV, further research is essential to extend the half-life of the antibodies, develop more potent antibodies and vector-based bNAbs for HIV prevention, and identify bNAb combinations that can suppress HIV long-term.

In addition to vaccine strategies, NIH will continue to pursue the development of other HIV prevention approaches, such as pre-exposure prophylaxis (PrEP). NIH has supported studies demonstrating that daily, oral antiretroviral therapy (ART)-based PrEP can reduce the risk of HIV acquisition by nearly 100 percent if taken as prescribed. For many people in the United States and globally, however, "a pill a day" is not optimal and adherence can be a challenge. Consequently, NIH is expanding research into long-acting formulations for PrEP (as well as for HIV treatment) including research into bNAbs and long-acting small molecules as antiretroviral agents. The goal is to develop PrEP options that require weeks or months between doses, rather than everyday dosing. In addition to product development, behavioral, social, and implementation sciences research is being supported to better understand how adherence to prevention interventions such as PrEP may be optimized for different populations.

PrEP is only administered to HIV-negative individuals. To determine HIV status in ways that are acceptable to people at risk of HIV infection, NIH is continuing to partner with organizations to develop new HIV testing technologies, in particular self-testing methods. Internal to NIH, this is being done in alignment with the priorities of the NIH Point-of-Care Technologies Research Network (POCTRN), housed within the National Institute of Biomedical Imaging and Bioengineering (NIBIB). OAR and a host of NIH ICOs support POCTRN activities, which aim to develop diagnostic technologies that are rapid, sensitive, specific, easy to use, and cost effective.

Budget Policy: The FY 2021 President's Budget request to reduce the incidence of HIV is $660.2 million, a decrease of $77.1 million or 10.5 percent compared to the FY 2020 Enacted level.

Develop Next-Generation HIV Therapies

NIH-sponsored research has led to the development of combination ART (cART) that has significantly improved the health outcomes, including the quality and length of life, of people with HIV. HIV infection has changed from a rapidly fatal disease to a chronic condition with treatment. Consistent use of cART reduces damage to the immune system by suppressing viral replication, delaying the development of viral resistance, and leading to undetectable viral loads, thereby preventing sexual transmission of HIV to an uninfected partner. However, even with simplified, effective daily one-pill treatment regimens capable of suppressing HIV, only 23 million (60 percent) of the approximately 38 million people with HIV worldwide currently receive treatment. Barriers to uptake and adherence to cART include treatment unavailability, high cost, the need for daily doses, interactions with other drugs, and the potential for drug

resistance and/or adverse events. In addition, stigma and disparities in access to cART adversely impact health outcomes in people with HIV across race, ethnicity, sex, gender, age, socioeconomic status and geographic location.

NIH will continue to support the development of new, long-acting HIV medications with fewer side effects and complications, including monthly injections of continuously released cART, a six-month cART implant, and anti-HIV antibody infusions. Ideally, new long-acting interventions should be highly effective, safe, user-friendly, suitably durable, inexpensive, socially acceptable, and easy to implement.

One major area for development of new therapeutic agents is bNAbs, originally discovered in the search for strategies for an effective vaccine. Over the last 5-10 years, significant advances have been made in isolating bNAbs and understanding how this class of antibodies develops in humans. NIH research is building on these advances by supporting clinical trials to verify the concept of passive bNAb infusions as a modality for HIV prevention, for longer-acting antiretroviral treatment, and for inducing sustained ART-free HIV remission. In parallel, research is supporting biotechnology strategies to engineer more potent and/or longer acting bNAbs, as well as antibodies better able to promote killing of HIV-infected cells as distinct from neutralizing circulating free virus.

An important factor in the development of any new therapeutic target is understanding the life cycle of HIV within the host cell. Currently, there are more than five classes of antiretroviral medications that target different points in the viral life cycle. New therapeutic targets will prevent HIV replication at additional stages in the viral life cycle, such as maturation, egress and necessary host interactions.

Budget Policy: The FY 2021 President's Budget request to develop next-generation HIV therapies is $313.1 million, a decrease of $52.5 million or 14.4 percent compared to the FY 2020 Enacted level.

Research Toward a Cure for HIV

Significant challenges to cure HIV continue because of the persistence of HIV as integrated DNA in latently infected cells and other reservoirs. To date, one individual has demonstrated long term ART-free suppression of HIV through a complex and costly bone marrow transplant procedure. While the outcome supports the possibility that cure of HIV ultimately may be achievable, focus now is on achieving long-term HIV suppression as a vital and essential step towards cure. Further fundamental research using novel technologies will be supported to characterize, quantify, eliminate or control the viral reservoir in different anatomical sites and cell types and to test the efficacy of novel cure strategies in appropriate animal models and human clinical trials.

NIH will invest in cure strategies with a "back to basics" approach that focuses on fundamental virology and cell biology. The aim is to better understand mechanisms of virus/host cell interactions that will lead to rational design of innovative strategies for extended viral suppression and ultimately viral elimination. Latent HIV reservoirs, DNA coding for HIV that

persists in people with HIV despite the use of cART, present a significant challenge to finding a cure. Reservoirs of HIV can be found in certain "sanctuary" sites in the body, including the brain, allowing the virus to hide and be protected from both the immune system and cART, preventing sustained, ART-free viral remission, viral eradication, and a permanent HIV cure.

Because the mechanisms that underlie reservoir dynamics are not well understood, NIH invests in basic research to identify, characterize, and eradicate HIV or to inhibit viral reactivation through novel approaches and treatments that target HIV reservoirs. A range of techniques, including single-cell and imaging technologies, are being used to identify and describe the HIV reservoir and discover mechanisms of viral reactivation from latently infected cells. Experimental treatments in development include therapeutic vaccines, genetically engineered immune cells that are resistant to HIV infection, drugs that reactivate latent HIV to make the virus visible to the immune system so that the virus can be cleared, cure-inducing immunotherapies, and interventions to prolong the time between antiretroviral treatments from one day to a few months or longer for an ART-free viral remission.

In parallel to basic and clinical research, NIH is supporting behavioral and social science research to ascertain what kind of cure strategies will be perceived as feasible and desirable among different groups of people with HIV. A core question under exploration is how the risks and benefits of potential HIV cure strategies (including participation in the associated research) are weighed, particularly in the context of living a healthy life and maintaining viral suppression under currently available, highly effective cART.

Budget Policy: The FY 2021 President's Budget request to promote research toward a HIV cure is $180.8 million, a decrease of $16.8 million or 8.5 percent compared to the FY 2020 Enacted level.

Address HIV-Associated Comorbidities, Coinfections and Complications

HIV infection affects and is affected by co-occurring infections, conditions, and non-communicable diseases. Among people with HIV, tuberculosis, viral hepatitis, and cancer are among the greatest causes of mortality, and the risk for comorbidities such as cardiovascular disease, some cancers, bone fractures/osteoporosis, liver disease, kidney disease, cognitive decline, and aging-related frailty is higher than among those without HIV. Additionally, treatment of cancer and other comorbidities can be complicated by co-existing HIV infection. Similarly, HIV often occurs concomitantly with other sexually transmitted infections (STI) and/or in association with alcohol, tobacco, and drug misuse, violence and trauma, and mental illness. Further research will be supported to better understand and address all of these co-occurring conditions.

Effective cART has ushered in a new era for the HIV epidemic. PWH can now achieve nearly normal lifespans, but are more likely to suffer from multiple, chronic comorbidities, coinfections, and complications resulting from virus exposure, long-term HIV disease, immune dysfunction, and/or cART for treatment or prevention, which can severely impact their quality of life. These include neurocognitive and cardiovascular complications, malignancies, metabolic and bone disorders, mental health impairments, substance use, and others. The overlapping etiologies and

consequences of HIV-associated diseases need to be better understood in order to improve the health and well-being of PWH across the lifespan.

While, traditionally, most ICO initiatives focus on diseases that fall within a specific ICO's mission, OAR will continue to encourage and support opportunities that will engage multiple ICOs to target the interrelationship among multiple comorbidities, co-infections that exacerbate prognosis and burden of disease, and the overall impact of HIV infection.

Budget Policy: The FY 2021 President's Budget request to address HIV-associated comorbidities, coinfections, and complications (CCCs) is $501.6 million, a decrease of $41.9 million or 7.7 percent compared to the FY 2020 Enacted level.

Cross-Cutting Areas

HIV epidemics often result from and provide a lens on social inequalities, stigma and discrimination, and health disparities that reflect factors such as sex, gender, race, ethnicity, socioeconomic status, age, sexual orientation and behavior, substance use behavior, and geographic location. NIH will continue to support research to better understand the social determinants of health – to improve HIV testing, engagement, retention in prevention and care services, and to enhance the health and wellbeing of persons living with and at risk for HIV in underserved and marginalized communities.

To maximize efficiencies and investments toward reaching global HIV pandemic control, NIH will support implementation science that includes purposeful blending of known and new methodologies of translational research, clinical effectiveness, and effective scale-up.

To ensure that the priority areas of HIV science are addressed with novel, innovative, and culturally responsive approaches, NIH will augment its commitment to the development of the next generation of HIV researchers, particularly those from underrepresented populations and institutions, by providing support for human resources and infrastructure.

Moving forward, NIH will continue to leverage advances in big data science, combine data sets from multiple cohorts, and utilize novel clinical trial designs to move the field forward across the NIH priorities for HIV and HIV-related research.

Budget Policy: The FY 2021 President's Budget request to address cross-cutting areas is $1,157.3 million, a decrease of $74.7 million or 6.1 percent compared to the FY 2020 Enacted level.

Programs and Activities to Support NIH's Highest Scientific Priorities

New NIH-Wide (and HHS-Wide) Initiatives

As stated earlier, the NIH HIV/AIDS Research Program is strategically aligned with the goals and timelines of three closely related domestic plans: NHAS, NVHAP, and EHE. OAR will

collaborate with its partners across NIH and HHS to ensure that the goals of the NIH HIV/AIDS Research Program complement and enhance these activities.

The four goals of the current NHAS are to: (1) reduce new HIV infections; (2) increase access to care and improve health outcomes for people with HIV; (3) reduce HIV-related health inequities; and (4) achieve a more coordinated national response to the HIV epidemic.[159] The OAR is actively engaged with the HHS Steering Committee in developing the next five-year (FY 2021–2025) NHAS strategy. Concurrent with the development of the updated NHAS, the NVHAP is being updated for FY 2021-2025 and aligned with the NHAS. The four goals of the current NVHAP are to: (1) prevent new viral hepatitis infections; (2) reduce death and improve the health of people living with viral hepatitis; (3) reduce viral hepatitis health disparities; and (4) coordinate, monitor, and report on implementation of viral hepatitis activities.[160]

The EHE initiative, first proposed in the President's 2020 Budget and announced during the President's State of the Union address in February 2019, aims to end the domestic HIV epidemic by 2030. To meet the goals of reducing new infections in the United States by 75 percent within five years, and then by 90 percent within 10 years, HHS will leverage critical scientific advances in HIV prevention, diagnosis, treatment, and care by coordinating the highly successful programs, resources, and infrastructure of the Centers for Disease Control and Prevention (CDC), NIH, Health Resources and Services Administration (HRSA), Substance Abuse and Mental Health Services Administration (SAMHSA), and Indian Health Service (IHS). The initiative is focused on geographic and demographic hotspots in 19 states, Washington, DC, and Puerto Rico, as well as in 7 states with a disproportionate occurrence of HIV in rural areas, where the majority of the new HIV cases are reported.[161]

The multi-year program will increase expertise, technology, and resources needed to end the HIV epidemic in the United States. The initiative has four pillars – (1) diagnose all people with HIV as early as possible after infection; (2) treat the infection rapidly and effectively to achieve sustained viral suppression; (3) protect people at risk for HIV using potent and proven prevention interventions, including pre-exposure prophylaxis (PrEP); and (4) respond rapidly to detect and respond to growing HIV clusters and prevent new infections. Activities related to these will be implemented across the entire United States within 10 years. Without this EHE initiative, new infections will continue to increase, costing more lives and the U.S. government more than $200 billion in HIV-associated direct lifetime medical costs. NIH's Centers for AIDS Research are the first step to increase research's best approaches in different communities to inform HHS partners based on state-of-the-art biomedical research findings, and by collecting and disseminating data on the effectiveness of approaches used. The FY 2021 budget includes an additional $10 million in funding, for a total of $16 million, to leverage the CFAR's pilot data to design and evaluate effective, sustainable systems for the implementation of prevention and treatment interventions, with a focus on implementing strategies at scale that will be the most effective.

Conclusion

[159] www.hiv.gov/federal-response/national-hiv-aids-strategy/nhas-update
[160] www.hhs.gov/hepatitis/viral-hepatitis-action-plan/index.html
[161] Fauci, et. al., Ending the HIV Epidemic – A Plan for the United States; JAMA 2019; 321:844-845

The HIV/AIDS research investment from the NIH continues to produce significant groundbreaking scientific advances, unprecedented opportunities, and exciting new challenges. NIH's leadership, commitment and dedication to strategically allocate funds to the highest research priorities are essential to successfully bring an end to the HIV/AIDS pandemic and the continuance to improve the quality of life for PWH. OAR will continue to coordinate HIV/AIDS efforts across all ICOs receiving HIV funding to make the most of NIH's and the public's investments.

DRUG CONTROL PROGRAMS

RESOURCE SUMMARY

	Budget Authority (in millions)		
	FY 2019 Final	FY 2020 Enacted	FY 2021 Request
Drug Resources by Function			
Research and Development: Prevention	$477.151	$446.883	$435.063
Research and Development: Treatment	$988.635	$1,070.760	$1,051.215
Total, Drug Resources by Function	**$1,465.786**	**$1,517.643**	**$1,486.278**
Drug Resources by Decision Unit			
National Institute on Alcohol Abuse and Alcoholism (NIAAA)			
Research and Development: Prevention	$51.208	$53.298	$48.485
Research and Development: Treatment	$6.362	$6.621	$6.023
National Institute on Drug Abuse (NIDA)			
Research and Development: Prevention	$425.943	$393.585	$386.578
Research and Development: Treatment	$982.273	$1,064.139	$1,045.192
Total, Drug Resources by Decision Unit	**$1,465.786**	**$1,517.643**	**$1,486.278**
Drug Resources Personnel Summary			
Total FTEs (direct only)	357	382	382
Drug Resources as a Percent of Budget			
Total Agency Discretionary Budget (in Billions) *	$37.9	$40.3	$37.7
Drug Resources percentage	3.87%	3.77%	3.94%

* The total agency discretionary budget includes amounts requested in FY 2021 for consolidation of activities of the Agency for Healthcare Research and Quality into NIH as the National Institute for Research on Safety and Quality (NIRSQ). NIRSQ does not have any programs classified as part of the National Drug Control Budget.

PROGRAM SUMMARY

MISSION

The National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two of the 27 Institutes and Centers of the National Institutes of Health (NIH), support research in pursuit of the objectives of the *National Drug Control Strategy*. NIDA funds research on the prevention and treatment of drug use, addiction, and its harmful consequences. NIDA is the lead federal agency supporting scientific research on drug use and its consequences, with a mission to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. NIDA accomplishes its mission through strategically supporting and conducting basic and clinical research on drug use (including nicotine), its consequences, and the underlying neurobiological, behavioral, and social mechanisms involved, and ensuring the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorders and enhance public awareness of addiction as a brain disorder. NIAAA's mission is to generate and disseminate fundamental knowledge about the

effects of alcohol on health and well-being, and apply that knowledge to improve diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder, across the lifespan. A major priority within NIAAA's mission is research on the prevention and treatment of underage drinking and its harmful consequences.

Substance use and substance use disorder (SUD) cost the United States more than $740 billion a year in healthcare, crime, and lost productivity;[162] but dollars cannot capture the devastating human cost of addiction to individuals, families, and communities. Drug overdose is now the leading cause of unintentional fatal injury in our nation. In 2017, more than 19.7 million Americans had substance use disorder (SUD),[163] and drug overdose claimed more than 70,000 lives, about two-thirds of which were from illicit or prescription opioids. For every fatal overdose it is estimated that there are 10 non-fatal overdoses and 20 opioid-related hospitalizations.[164]

Studying substance misuse, SUD, and their causes is a complex challenge compounded by societal stigma and misunderstanding that many other illnesses do not face. The landscape of drug use and addiction in America evolves from year to year; a decades-long prescription opioid overdose epidemic led to a rise in heroin deaths, and now overdose from synthetic opioids such as fentanyl and carfentanil predominates. The rising use of synthetic drugs as well as new drug delivery systems such as electronic cigarettes (e-cigarettes) are changing how people use drugs. New HIV and Hepatitis C outbreaks have arisen as a byproduct of intravenous drug use. In addition, the line between legal and illegal substance use has blurred as a growing number of states are legalizing marijuana for recreational and medical use. This presents an opportunity to study the outcomes of these policy changes as natural experiments.

NIDA is supporting research to address today's drug use-related challenges in several key areas, including supporting the Secretary of HHS in responding to opioid misuse, addiction, and overdose; spearheading a landmark longitudinal study of adolescent substance use (including vaping) and brain development in collaboration with NIAAA and other Federal partners; studying the impact of new synthetic drugs; studying the impact of marijuana use; supporting development of new treatments for stimulant addiction; and contributing to scientific and public understanding of the brain mechanisms underlying addiction. These projects represent a significant contribution to the *National Drug Control Strategy*.

Opioid misuse, addiction, and overdose is an ongoing and rapidly evolving public health crisis. Millions of Americans have an opioid use disorder (OUD), and millions more suffer from chronic pain. The urgency and scale of this crisis call for innovative scientific solutions. As part of a government-wide effort to address the opioid crisis, the NIH launched the NIH HEAL (Helping to End Addiction Long-term^{SM}) Initiative in April 2018. The HEAL Initiative is an aggressive effort to speed scientific solutions to stem the national opioid public health crisis, bolstering research to develop and improve treatments for opioid misuse and addiction and to enhance pain management.

[162] https://www.drugabuse.gov/related-topics/trends-statistics
[163] 2017 National Survey on Drug Use and Health, 2018. SAMHSA.
[164] Rudd, R. et al. MMWR Morb. Mortal. Wkly. Rep. 65, 1445-1452, (2016).

Alcohol misuse has profound effects on the health and well-being of individuals, families, and communities, costing the United States an estimated $249 billion per year. NIAAA is committed to reducing the burden of alcohol misuse for individuals at all stages of life and supports a diverse portfolio of research to elucidate the effects of alcohol on health. Research areas include biological and behavioral mechanisms underlying alcohol misuse, alcohol use disorder (AUD), and alcohol-related health conditions; epidemiological assessments of patterns and trends in alcohol use; and the development and evaluation of interventions to diagnose, prevent, and treat alcohol misuse and its consequences, including among youth. NIAAA also supports efforts to translate research findings to improve prevention and treatment of alcohol-related problems and co-occurring conditions and to disseminate evidence-based information to health care providers, researchers, policy makers, and the public. These ongoing efforts have significantly broadened our understanding of AUD, helping to reduce stigma, and provided support for integrating alcohol prevention and treatment services into mainstream health care.

METHODOLOGY

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

The prevention and treatment components of NIAAA's underage drinking research program are classified as a part of the National Drug Control Budget. Underage drinking research is defined as research that focuses on alcohol use by youth (individuals under the legal drinking age of 21), as well as the negative consequences of underage alcohol use (e.g., alcohol-related injuries, impact on adolescent development including on the developing brain, and risk for AUD). It includes basic biological and behavioral research, epidemiological research, screening studies, the development and testing of preventive and treatment interventions, and efforts to disseminate evidence-based information. NIAAA's methodology for developing budget estimates for the Budget and Performance Summary is a two-step process. First, NIAAA identifies its underage drinking projects using NIH's automated, electronic text mining system for research, condition, and disease categorization. Once these projects are verified as underage drinking projects, NIAAA conducts a manual review of the project listing and codes each verified project as relevant to prevention or treatment.

BUDGET SUMMARY

The FY 2021 request for drug-related activities at NIH is $1,486.3 million ($1,431.8 million for NIDA and $54.5 million for NIAAA), a 2.1 percent decrease compared with the FY 2020 Enacted level.

NIH-supported research has provided and will continue to provide the scientific basis for drug control policy. For example, NIH continues to explore the many biological, behavioral, and environmental influences on substance misuse and addiction vulnerability, which will allow the development of more targeted and effective prevention approaches. Research reveals that universal prevention programs not only reduce drug use, underage drinking, and other risky behaviors that can lead to HIV and other adverse outcomes, but can also promote other positive outcomes, such as strengthening young people's sense of community or "connection" to school—key to reducing substance misuse, violence, and mental health problems.

Another top priority continues to be the development and deployment of therapeutic interventions to treat SUD, including medications, biologics, behavioral interventions, and non-pharmacological interventions such as transcranial magnetic stimulation or neurofeedback. NIH is now poised to capitalize on a greater understanding of the neurobiology underlying addiction, and of newly identified candidate molecules and brain circuits that show promise as potential targets for the treatment of SUD. However, discovering new therapies is not sufficient to combat SUD if these therapies do not reach the people who need them. In many cases, such as medications for the treatment of OUD (MOUD), studies suggest that effective treatments are under-utilized despite strong evidence of their effectiveness. To address this issue, NIH is also exploring ways of improving the dissemination and implementation of evidence-based practices (implementation science) in real world settings to improve the prevention and treatment of SUD and co-occurring conditions such as HIV and psychiatric disorders, thereby enhancing the public health impact of NIH-supported research.

In April 2018, NIH launched the HEAL Initiative (see above), an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. This Initiative will build on extensive, well-established NIH research, including basic science of the complex neurological pathways involved in pain and addiction, implementation science to develop and test treatment models, and research to integrate behavioral interventions with MOUD.

As part of the NIH HEAL Initiative, NIDA (and to a lesser extent, NIAAA) supports a variety of projects aimed at advancing our understanding of how to prevent and treat opioid misuse and addiction and reverse opioid overdose. This includes research studies focused on:

- Enhancing the NIDA Clinical Trials Network to Address Opioids[165]
- Focused Medication Development to Treat Opioid Use Disorder and Prevent/Reverse Overdose[166]
- Determining strategies to reduce opioid overdose in communities hardest hit by the opioid crisis (the HEALing Communities Study)[167]

[165] https://heal.nih.gov/research/research-to-practice/enhancing-clinical-trials-network
[166] https://heal.nih.gov/research/medication-options/focusing-development
[167] https://heal.nih.gov/research/research-to-practice/healing-communities

- Determining ways to improve the effectiveness and adoption of interventions within justice systems. (The Justice Community Opioid Innovation Network)[168]
- Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder[169]
- Prevention of Progression to Moderate or Severe Opioid Use Disorder [170]
- Optimizing the Duration, Retention, and Discontinuation of Medication Treatment for Opioid Use Disorder[171]
- Studying the effects of environmental factors, including opioids and other substance use, on early brain development from pregnancy through early childhood (HEALthy Brain and Child Development Study)[172]

National Institute on Drug Abuse
FY 2021 Request: $1,431.8 million
($26.0 million below the FY 2020 Enacted Level)

NIDA's efforts consist of Neuroscience and Behavioral Research; Epidemiology, Services and Prevention Research; Therapeutics and Medical Consequences; Clinical Trials Network; High-Tech Biomedical Product Development; Responding to the Opioid Crisis; Intramural Research Program (IRP); and Research Management and Support (RMS). The section entitled "Responding to the Opioid Crisis" details how NIDA is using dollars budgeted to the HEAL Initiative for the purpose of opioid research, but those dollars supplement base funding for opioid and pain research that are included within other NIDA program areas. Funding for both the HEAL initiative and other opioid and pain research will be held flat at the FY 2020 Enacted level within NIDA's overall FY 2021 request. In addition, FY 2021 funding includes $50.0 million for research to develop medication-assisted treatment and evidence-based psychosocial treatment to support the strategy to reduce the use of methamphetamines.

Neuroscience and Behavioral Research
FY 2021 Request: $456.4 million
($10.1 million below the FY 2020 Enacted Level)

NIDA's Division of Neuroscience and Behavior (DNB) funds a research portfolio focused on advancing knowledge of the fundamental molecular, genetic/epigenetic, cellular, neurological, pharmacological, cognitive and behavioral processes that underlie SUD and its co-occurring conditions such as HIV. This includes identifying the effects of addictive substances on brain structure and function throughout the lifespan and across stages of drug use and SUD, from first exposure through abstinence, relapse, and recovery. Central to these goals are efforts to delineate the multiple biological (e.g., genes, epigenetic modifications, neural substrates, development) and environmental (e.g., stress, social, childhood adversity) factors that contribute to drug use, physical dependence, and SUD risk. Areas of emphasis include studies to identify genetic variants and epigenetic modifications that influence vulnerability to SUD, the effects of

[168] https://heal.nih.gov/research/research-to-practice/jcoin
[169] https://heal.nih.gov/research/new-strategies/at-risk-adolescents
[170] https://heal.nih.gov/research/new-strategies/prevent-progression
[171] https://heal.nih.gov/research/new-strategies/duration-retention-discontinuation
[172] https://heal.nih.gov/research/infants-and-children/healthy-brain

addictive substances on gene expression and brain development and function; the interaction of genes with environmental conditions, such as stress and early exposure to drugs that influence risk for SUD; and basic processes underlying resilience against SUD. DNB supports research to elucidate the pharmacology of drugs with respect to their molecular interactions with receptors, ion channels and other proteins and intracellular signaling pathways and to leverage this knowledge towards the development of therapeutics to treat SUD, the adverse consequences of addictive substances, and pain. The DNB portfolio also includes research on non-pharmacological SUD treatments including transcranial magnetic stimulation, transcranial direct current stimulation, deep brain stimulation, and neurofeedback. DNB funds technology development that enables studies of the functional organization of the living brain—from cells to networks. This includes the interactions of complex neural circuits, the encoding of reward, craving, compulsive behavior, decision-making that may drive substance use, as well as the aversive responses to drugs that can inhibit drug-seeking. Advanced computational approaches, including theoretical modeling and novel methods for analyzing large, diverse data sets that enable the integration and simultaneous analysis of experimental data to better understand the neurobiological and behavioral consequences of drug use and SUD, are supported by DNB. Finally, DNB supports mechanistic research towards addressing real-world challenges faced in clinical care of SUD, such as polysubstance use and comorbid psychiatric disorders. Spanning these areas of interest is research into how sex/gender and individual differences affect the SUD trajectory, including risk, resilience, and recovery and the basic neurobiology underlying SUD. Collectively, the research supported by DNB shapes perspectives on the effects of drugs on multiple biological systems and advances knowledge of the basic biological mechanisms that underlie drug use, thus guiding the development of novel prevention strategies and therapies for SUD.

NIDA's portfolio also includes basic research to understand trajectories of substance use and its effects across the lifespan, funded by the Division of Extramural Research. Under the Collaborative Research on Addiction at the NIH (CRAN) partnership, NIDA, NIAAA, and the National Cancer Institute, along with other components of the NIH and the Centers for Disease Control and Prevention (CDC), are supporting a longitudinal study to examine how substance use affects neural development and identify factors that make adolescents vulnerable to SUD. The Adolescent Brain Cognitive Development (ABCD) study will follow the development of more than 10,000 children over 10 years beginning at ages 9-10. Scientists will use techniques including advanced brain imaging, interviews, and behavioral testing to determine how childhood experiences interact with each other and with a child's changing biology to affect brain development and—ultimately—social, behavioral, academic, and health outcomes, including substance use and SUD. The ABCD study has enrolled 11,878 participants, meeting its recruitment target. Data on the first roughly 4,500 participants were released to the scientific community in February 2018; a comprehensive baseline dataset was released in April 2019.

Epidemiology, Services, and Prevention Research
FY 2021 Request: $326.2 million
($7.3 million below the FY 2020 Enacted Level)

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR or the Division) supports integrated approaches to understanding and addressing the interactions between

individuals and environments that contribute to drug use, addiction, and related health problems. Through Monitoring the Future and other studies, DESPR is also monitoring trends in vaping and e-cigarette use, and the potential risks and health outcomes related to these behaviors. DESPR also supports research on integrating prevention and treatment services into healthcare and community systems to reduce the burden of drug problems across the lifespan. For example, ongoing research is exploring SUD treatment in the justice system, including studies on implementation of medications for opioid use disorder and strategies for finding and screening people with SUD who are also at risk for HIV, as well as strategies for retaining them in treatment. NIDA also funds research into the efficacy of screening, brief intervention, and referral to treatment in primary care settings for reducing drug use and SUD. Other program efforts focus on research to optimize implementation of evidence-based prevention interventions and treatment services in real-world settings. For instance, NIDA is funding researchers to partner with states as they use the State Targeted Response funding provided to the Substance Abuse and Mental Health Services Administration (SAMHSA) in the 21st Century Cures Act to test approaches for expanding access to MOUD and naloxone for the reversal of overdose.

NIDA partnered with the Appalachian Regional Commission, the CDC, and SAMHSA to issue nine grants to help communities develop comprehensive approaches to prevent and treat consequences of opioid injection, including SUD, overdose, HIV, hepatitis B and C viral infections, as well as sexually transmitted infections. Funded in FY 2017, these projects work with state and local communities to develop best practice responses that can be implemented by public health systems in the nation's rural regions.

Therapeutics and Medical Consequences
FY 2021 Request: $134.8 million
($3.0 million below the FY 2020 Enacted Level)

NIDA's Division of Therapeutics and Medical Consequences (DTMC) supports preclinical and clinical research focused on developing treatments for SUD. Since the pharmaceutical industry has traditionally made limited investments in this area, the responsibility for supporting the development of therapeutics has rested largely with NIDA. To most effectively leverage NIDA resources, DTMC encourages the formation of partnerships among pharmaceutical and biotechnology companies, academic institutions, and other stakeholders with the common goal of expeditiously advancing new and repurposed compounds through the medications development pipeline toward FDA approval. For example, in collaboration with US WorldMeds, DTMC supported clinical trials on LUCEMYRA™, the first medication targeted specifically to treat the physical symptoms associated with opioid withdrawal. Having been shown to be safe and effective at managing withdrawal in patients discontinuing opioid use under medical supervision, LUCEMYRA™ was approved by the FDA in May 2018. NIDA also supports research to reduce the medical risks of compounds and to make them more feasible for pharmaceutical companies to complete costly phase IIb and III clinical studies for SUD indications.

Clinical Trials Network
FY 2021 Request: $40.1 million
($0.9 million below the FY 2020 Enacted Level)

The overarching mission of the NIDA Clinical Trials Network (CTN) is to allow medical and specialty treatment providers, treatment researchers, patients, and NIDA to cooperatively develop, validate, refine, and deliver new treatment options to patients. The CTN comprises: 18 research nodes with 34 principal investigators affiliated with academic medical centers and large health care networks; 2 research coordinating centers; and more than 240 community-anchored treatment programs and/or medical settings in over 40 States plus the District of Columbia and Puerto Rico. This unique partnership enables the CTN to conduct studies of behavioral, pharmacological, and integrated treatment interventions in rigorous, multisite clinical trials to determine effectiveness across a broad range of settings and patient populations. It also allows the CTN to ensure the transfer of research results to physicians, clinicians, providers, and patients. The network evaluates interventions, implementation strategies, and health system approaches to addressing SUD and related disorders, such as co-occurring mental health disorders and HIV.

The CTN is conducting studies to evaluate strategies for integrating OUD screening and treatment into emergency departments, pharmacies, primary care clinics, and American Indian/Alaska Native communities. It has also supported studies to capture important data for research on SUD in electronic health record (EHR) systems in primary care and emergency departments. The CTN is currently developing and testing a clinical decision support tool that integrates with EHR systems to help doctors diagnose OUD and either provide treatment or refer patients to appropriate treatment. Additional studies are investigating the effectiveness and safety of a combination pharmacotherapy for treatment of methamphetamine use disorder, assessing the effectiveness of OUD treatments for HIV-positive individuals with OUD, and improving the ability of healthcare providers to detect and address cocaine use using smartwatch technology. The CTN is also developing studies to examine the effects of medications for OUD in pregnant women and the effects of medical cannabis use using EHR data.

High-Tech Biomedical Product Development
FY 2021 Request: $38.3 million
($0.9 million below the FY 2020 Enacted Level)

NIDA's Office of Translational Initiatives and Program Innovations (OTIPI) takes research discoveries in prevention, detection, and treatment of SUD into candidate health applications for commercialization. Addiction (moderate to severe SUD) represents an underserved market, and OTIPI works to support early-stage commercialization of products in this area. OTIPI manages NIDA's Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) Programs, utilizing novel fit-for-purpose funding authorities such as Prizes and Open Competitions, and establishing teaching programs that equip scientists with the competence to translate advances in addiction research into tangible solutions that our society needs.

Many of these efforts take the form of innovative new technology applications, from mobile apps that help patients find open beds in addiction treatment facilities or connect to support communities, to more sophisticated medical devices. Among OTIPI-funded technologies are: hospital bassinets delivering calming signals to infants with neonatal abstinence syndrome; alarms for detecting the early signs of a drug overdose; and virtual reality systems to manage pain and reduce opioid analgesic use.

Responding to the Opioid Crisis
FY 2021 Request: $266.3 million
(Unchanged from the FY 2020 Enacted Level)

As part of HEAL, NIDA will continue to expand its support for new research efforts to combat opioid addiction with several major projects which began or ramped up in FY 2019 with continued support into FY 2020 and FY 2021.

NIDA supports research to accelerate the development of novel medications and devices to treat all aspects of the opioid addiction cycle, including progression to chronic use, withdrawal symptoms, craving, relapse, and overdose. This includes developing longer-acting formulations of existing addiction medications to promote adherence to treatment while preventing medication misuse, as well as developing stronger, longer-acting formulations of opioid antagonists (including longer-lasting naloxone formulations and novel compounds) to reverse opioid overdose. The following projects are currently underway:

Enhancing the NIDA Clinical Trials Network to Address Opioids
To expand NIH research to more communities in areas of the country that are severely impacted by the opioid crisis, NIH is expanding the National Drug Abuse Treatment Clinical Trials Network (CTN). The Network facilitates collaboration between government researchers, scientists at universities, and treatment providers in local communities with the aim of developing, testing, and implementing new addiction treatments. Through its work to date, the Network has contributed to broad-reaching changes in medical practice, including the development of the OUD treatment medication buprenorphine.

Focused Medication Development to Treat Opioid Use Disorder and Prevent/Reverse Overdose
More flexible treatment options for opioid use disorder (OUD) are needed to promote long-term recovery in more patients. Methadone, buprenorphine, and naltrexone are approved by the FDA to treat OUD, and lofexidine is approved to treat opioid withdrawal, but many people do not receive these medications or take them for only a short time, making it difficult to achieve long-term recovery. Naloxone can effectively reverse opioid overdose, but multiple doses can be required to reverse respiratory arrest caused by drug combinations or powerful synthetic opioids. NIDA is conducting a series of targeted studies with the goal of producing approximately 15 Investigational New Drugs (INDs) and 5 New Drug Applications (NDAs) submitted to the FDA. This project will accelerate the development of novel medications and devices to treat all aspects of the opioid addiction cycle, including progression to chronic use, withdrawal symptoms, craving, relapse, and overdose.

Determining strategies to reduce opioid overdose in communities hardest hit by the opioid crisis (the HEALing Communities Study)

The HEALing Communities Study will generate evidence about how tools for preventing and treating opioid addiction are most effective at the local level. NIH, together with SAMHSA, has launched this multisite implementation research study to test the impact of an integrated set of evidence-based interventions across healthcare, behavioral health, justice, and other community-based settings. The goal is to prevent and treat opioid misuse and opioid use disorder (OUD) within highly affected communities in 4 states and reduce opioid related deaths by 40 percent over 3 years. Each site is partnering with at least 15 communities to measure the impact of these efforts.

The Study will also look at the effectiveness of coordinated systems of care designed to reduce overdose fatalities and events; decrease the incidence of OUD; increase the number of individuals receiving medication to treat OUD, retained in treatment, and receiving post-treatment recovery support services; and increase the distribution of naloxone. The HEALing Communities Study provides funding to four academic institutions, in partnership with local community-based organizations.

Determining ways to improve the effectiveness and adoption of interventions within justice systems. (The Justice Community Opioid Innovation Network)

Many individuals with OUD pass through the criminal justice system over the course of their life. Improved access to high-quality, evidence-based addiction treatment in justice settings will be critical to addressing the opioid crisis. Through the Justice Community Opioid Innovation Network (JCOIN), NIH will study approaches to increase high-quality care for people with opioid misuse and OUD in justice populations. The Network will test strategies to expand effective treatment and care in partnership with local and state justice systems and community-based treatment providers.

Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder

Older adolescents and young adults (ages 16-30) are the group at highest risk for initiation of opioid use, opioid misuse, OUD, and death from overdose. Building on successful research models to prevent alcohol consumption among adolescents and young adults, NIH is supporting a series of studies to identify and test effective prevention strategies targeted to young adults in geographic areas most affected by the opioid crisis. The studies will focus on older adolescents and young adults in a variety of health care settings, including primary care, emergency departments, urgent care, infectious disease clinics, school-based and community college health centers, workplaces, and justice settings.

Prevention of Progression to Moderate or Severe Opioid Use Disorder

There are currently multiple evidence-based strategies for the treatment of OUD. And yet, OUD develops over time, beginning with opioid use and misuse below the threshold for the clinical diagnosis for OUD. Historically, low severity opioid misuse, especially in the context of co-occurring pain and psychiatric disorders, has been poorly identified in clinical settings. To understand how to prevent the transition from opioid misuse to more severe opioid use disorder,

NIH will develop and test effective intervention strategies for persons with low severity opioid misuse, including patients with pain.

This study will recruit individuals with sub-threshold and low-severity opioid use disorder in general medical settings such as primary or integrated care settings to define, identify, and intervene in the management of opioid misuse. The study will test a model including (1) a practice-embedded nurse care manager who provides patient education and supports the primary care provider (PCP) in engaging and monitoring patients who have unhealthy opioid use; (2) brief advice delivered to patients by their PCP; and (3) counseling of patients by health coaches and mental health providers to motivate and support behavior change.

Optimizing the Duration, Retention, and Discontinuation of Medication Treatment for Opioid Use Disorder

Effective medications for treating OUD exist; patients have better outcomes with longer periods of treatment, and risk of relapse increases when patients stop taking medication. Better strategies are needed to retain patients in treatment, and little is known about when it may be safe to discontinue medications. This study will test strategies to improve retention in medication-based treatment for OUD as well as strategies to improve outcomes among patients who have been stabilized on OUD medications and want to stop taking medication. The research will also identify patient characteristics associated with relapse after discontinuation and develop a predictive risk model for relapse.

Studying the effects of environmental factors, including opioids and other substance use, on early brain development from pregnancy through early childhood (HEALthy Brain and Child Development Study) (https://heal.nih.gov/research/infants-and-children/healthy-brain)

The first few years of life is a period of exponential brain growth and development. It is not currently known how infant and childhood development is affected by early exposure to opioids. To address this question, NIH is working to better understand typical brain development, beginning in the prenatal period through early childhood, including variability in development and how it contributes to cognitive, behavioral, social, and emotional function. Knowledge of normative brain trajectories is critical to understanding how brain development may be affected by exposure to opioids and other substances (e.g., alcohol, tobacco, cannabis), stressors, trauma and other significant environmental influences.

The HEALthy Brain and Child Development (HBCD) Study will establish a large cohort of pregnant women from regions of the country significantly affected by the opioid crisis, and follow them and their children for at least 10 years. Research from this cohort will help researchers understand normative childhood brain development as well as the long-term impact of pre- and postnatal opioid and other drug and adverse environmental exposures. The study will collect data on pregnancy and fetal measures; infant and early childhood structural and functional brain imaging; anthropometrics; medical history; family history; biospecimens; and data on social, emotional, and cognitive development. This knowledge will be critical to help predict and prevent some of the known impacts of pre- and postnatal exposure to certain drugs or adverse environments, including risk for future substance use, mental disorders, and other behavioral and developmental problems.

Intramural Research Program
FY 2021 Request: $98.0 million
($2.2 million below the FY 2020 Enacted Level)

In addition to funding extramural scientists, NIDA conducts research in high priority areas through its Intramural Research Program (IRP). The IRP conducts multidisciplinary cutting-edge research to: 1) elucidate the mechanisms underlying the development of SUD; 2) evaluate potential new therapies for SUD, including pharmacological and non-pharmacological interventions (e.g., psychosocial, neurofeedback, brain stimulation technologies, mobile health tools); and 3) identify and pharmacologically characterize emerging designer drugs such as synthetic opioids, stimulants, and cannabinoids, providing data-based evidence to the public on the dangers of these drugs.

One example of treatment evaluation at the IRP is a bench-to-bedside project in which IRP investigators are testing a novel compound to treat OUD. The compound activates the same receptors as traditional opioids, but has only a subset of their cellular actions. IRP investigators are testing whether the compound reduces self-administration of opioids in a variety of animal models and, in parallel studies in people with OUD, whether it prevents opioid withdrawal with fewer side effects than treatment drugs in current use. If trials prove successful, this compound could be a new medication for OUD.

The IRP is also working with the National Center for Advancing Translational Sciences on a dopamine D3 receptor antagonist that could be taken together with opioid pain relievers to reduce the chance of developing OUD. Preliminary animal studies have suggested that the compound reduces opioid self-administration and drug-seeking behavior without reducing the pain-relieving effects of opioids. This compound holds promise as an adjunct to opioid treatment for pain, and evidence suggests it could also be useful as a treatment for OUD.

Non-pharmacological addiction treatments are also being developed at NIDA. Research at the IRP's on-site treatment-research clinic includes efforts to develop a smartphone app that detects or predicts stress, craving, and drug use via machine learning, on a time scale of hours—and a parallel project to develop the content that the app should deliver in a "just in time" fashion. Currently marketed apps purporting to serve these functions do not meet scientific standards of evidence for either their content or their risk-detection methods. The IRP is addressing that major gap in mobile health. Using passive measurement and digital phenotyping techniques, the IRP is also developing interventions and big data methodologies to prevent HIV transmission associated with high-risk sexual behavior in the context of substance use.

Research Management and Support
FY 2021 Request: $71.5 million
($1.6 million below the FY 2020 Enacted Level)

Research Management and Support (RMS) activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. Additionally, the functions of RMS encompass strategic planning, coordination, and evaluation of NIDA's programs, regulatory compliance,

international coordination, and liaison with other Federal agencies, Congress, and the public. RMS staff at NIDA play leadership roles in helping to coordinate NIDA's involvement in the NIH HEAL Initiative, spearheading NIH's response to the opioid overdose epidemic. In addition to the infrastructure required to support research and training, NIDA strives to provide evidence-based resources and educational materials about substance use and addiction, including information about timely public health topics such as opioid overdose prevention, marijuana research, use and consequences of vaping, synthetic drug trends, and medications for treatment of SUD including OUD.

The RMS portfolio also incorporates education and outreach activities to inform public health policy and practice by ensuring that NIDA is the primary trusted source for scientific information on drug use and addiction. Staff supported by NIDA's RMS budget coordinate key activities that help to train the next generation of scientists and clinicians in the science of addiction and evidence-based approaches to treatment and prevention. In addition, NIDA's RMS portfolio includes the NIDAMED initiative, which is aimed at engaging and educating clinicians in training and in practice in the latest science related to drug use and addiction.

National Institute on Alcohol Abuse and Alcoholism
FY 2021 Request: $54.5 million
($5.4 million below the FY 2020 Enacted Level)

NIAAA's underage drinking portfolio includes studies to develop, evaluate, and implement evidence-based prevention programs for underage and college drinking. These include individual-, family-, school-, community-, and environmental-level interventions for underage individuals at large, as well as those designed or adapted for specific populations and settings. The college environment remains a high priority target for reducing underage drinking. NIAAA developed the College Alcohol Intervention Matrix (CollegeAIM) to assist college and university officials in addressing alcohol misuse on their campuses. CollegeAIM is a user-friendly guide and website that rates nearly 60 evidence-based alcohol interventions in terms of effectiveness, cost, and other factors, allowing school officials to select among the many potential interventions to address harmful and underage student drinking.

Although the prevalence of alcohol use among 8th, 10th, and 12th graders has declined by one-third over the past decade, alcohol remains the most widely used substance among U.S. youth. Binge drinking[173] and high intensity drinking (i.e., two or more times the gender-specific binge drinking thresholds) among young people remain significant concerns; these practices are particularly troubling as they increase risks for poor academic performance, alcohol-related blackouts, injuries, overdoses, sexual assault, unsafe sexual behavior, AUD, and other detrimental consequences. NIAAA recently convened an expert panel to better understand the biological and social determinants of high-intensity drinking to inform NIAAA efforts in moving this area of research forward.

NIAAA also supports research on the implementation of alcohol screening and brief intervention among youth and young adult populations in health care and other appropriate settings. Alcohol

[173] NIAAA defines binge drinking as a pattern of drinking that increases an individual's blood alcohol concentration to 0.08 percent or higher. This typically occurs after 4 drinks for women and 5 drinks for men – in about 2 hours.

screening and brief intervention in primary care has been recognized as a leading preventive service for reducing harmful alcohol use in adults, and a growing body of evidence demonstrates its effectiveness in preventing and reducing alcohol misuse in youth. However, adolescents are not routinely asked about drinking when they interface with the health care system. To facilitate the integration of this practice into primary care, NIAAA developed a youth alcohol screening tool to enable pediatric and adolescent health practitioners to identify patients who may benefit from intervention. This screening tool has been validated among youth in pediatric emergency room settings, in school settings, in primary care settings with racially and ethnically diverse youth, and among youth with chronic health conditions.

Basic research is key to informing the development of innovative prevention and treatment strategies for underage drinking. NIAAA funds collaborative research to assess the impact of adolescent drinking on brain development. For example, the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a longitudinal study of approximately 800 youth ages 12-21, was designed to identify brain characteristics that may predict alcohol-misuse and to elucidate the neurodevelopmental effects that occur as a consequence of alcohol exposure. NCANDA researchers have demonstrated that youth with a history of alcohol use exhibit weakened connections between brain networks involved in the regulation of emotional and cognitive functioning. NCANDA laid the methodological foundation for NIH's Adolescent Brain Cognitive Development (ABCD) study, the largest longitudinal study of brain development and child health in the United States. Complementing NCANDA and ABCD, NIAAA's Neurobiology of Adolescent Drinking In Adulthood (NADIA) consortium enables investigators to examine, using animal models, the mechanisms by which adolescent drinking leads to changes in brain structure and function that persist into adulthood. Recent preclinical research conducted through NADIA elucidated a link between adolescent alcohol exposure and specific molecular changes in the brain that contribute to increased anxiety in adulthood.

PERFORMANCE

Information regarding the performance of the drug control efforts of NIH is based on agency documents related to the Government Performance and Results Modernization Act and other information that measures the agency's contribution to the *Strategy*. NIH's performance measures are representative of Institute contributions to NIH's priorities regarding specific scientific opportunities, identified public health needs, and Presidential priorities. Such measures, reflecting NIH's broad and balanced research portfolio, are not Institute-specific. Many measures are trans-NIH, encompassing lead and contributing Institutes and Centers. This approach reflects NIH's commitment to supporting the best possible research and coordination of research efforts across its Institutes and Centers.

NIDA and NIAAA lead and support a number of trans-NIH measures in the Scientific Research Outcome (SRO) functional area. While NIDA and NIAAA engage in many research and related activities, four measures best reflect the breadth of their efforts in the prevention and treatment of substance use, misuse, addiction, and its consequences.

One of these measures, led by NIAAA and supported by NIDA, is SRO-5.15: "By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations." This measure, which began in FY 2014, is indicative of NIAAA's and NIDA's efforts to support research to foster the development and implementation of prevention-based strategies for reducing substance misuse and addiction. NIH's prevention portfolio encompasses a broad range of research on the efficacy and cost effectiveness of primary prevention programs—designed to prevent substance use before it starts, or prevent escalation to misuse or addiction—and how these programs can be enhanced by targeting prevention efforts toward populations with specific vulnerabilities (genetic, psychosocial, or environmental) that affect their likelihood of substance use or SUDs.

NIDA created and leads SRO-4.9: "By 2020, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD)." This measure began in FY 2018, and reflects NIDA's increasing focus on finding solutions to the current crisis of opioid overdose and addiction. As part of the NIH HEAL Initiative, NIDA has been supporting a variety of focused medications development research at varying stages of the clinical pipeline.

In addition to developing and leading SRO-5.15, NIAAA created SRO-4.15: "By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations." This measure began in FY 2019 and reflects NIH's ongoing commitment to research on the development of interventions to improve treatment of alcohol-related problems among youth.

National Institute on Drug Abuse		
Selected Measures of Performance	**FY 2019 Target**	**FY 2019 Achieved**
Scientific Research Outcome-5.15: By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations.	Develop, adapt or tailor at least one intervention or strategy to prevent prescription drug misuse and/or OUD in older adolescent and young adult populations.	NIDA supported at least three projects focused on developing, tailoring and/or adapting interventions to prevent prescription drug misuse and/or OUD in older adolescent and young adult populations.
Scientific Research Outcome-4.9: By 2020, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD).	Conduct 1 pre-clinical study and 1 clinical trial to develop non-opioid based medications to treat OUD that may avoid the risks of opioid dependence and overdose.	A pre-clinical study of a novel opiate withdrawal therapy was conducted, and a clinical trial of a therapy for both opioid withdrawal and associated insomnia was also conducted.

Prevention – Scientific Research Outcome-5.15
The FY 2019 target was met. In FY 2019 NIDA supported at least three projects focused on developing, tailoring and/or adapting interventions to prevent prescription drug misuse and/or OUD in older adolescent and young adult populations.

NIDA supported a project[174] which intervenes at the level of the patient, aiming to improve opioid risk understanding and analgesic decision-making and to enhance analgesic self-efficacy, analgesic use, storage behaviors and pain outcome. The project tests the effectiveness of targeting parents of children who have been prescribed opioids for acute pain with new strategies to help parents learn about opioid risks, make safe and effective analgesic decisions, and develop and demonstrate safe drug management behaviors.

NIDA also supported two projects that are examining interventions at the level of the provider testing strategies to change prescribing behavior. One project[175] focuses on a behavioral intervention for providers that alters the default settings for prescribing opioids to children and young adults after common childhood surgical procedures like tonsillectomy. Another study[176] seeks to reduce the number of opioids prescribed after caesarian section, in order to reduce the prescription of unused opioids and reduce the potential for friends and family members to obtain and misuse such opioids.

[174] "Scenario tailored opioid messaging program: An interactive intervention to prevent analgesic-related adverse drug events in children and adolescents", R01-DA044245
[175] "Using default opioid prescription settings to limit excessive opioid prescribing to adolescents and young adults" K08DA048110
[176] "Reducing unused prescribed opioids after Cesarean Birth" K23DA047476

While it is too early for these studies to have produced published findings, each represents a NIDA's commitment to finding novel approaches to prevent opioid misuse prevention.

Treatment – Scientific Research Outcome-4.9
The FY 2019 target was met. In FY 2019, NIDA funded the preclinical development of ITI-333. This is a novel compound with high affinity activity at mu opioid (MOP), 5-HT2A, and D1 receptors. The pre-clinical profile of ITI-333 suggests a promising medication, lacking addiction liability, for treatment of opioid withdrawal in individuals with OUD. ITI is currently completing Investigational New Drug (IND)-enabling nonclinical safety, toxicology, pharmacokinetic and manufacturing activities to start studies in humans (clinical trials).

NIDA also funded a clinical trial to evaluate the safety and efficacy of suvorexant for treatment of insomnia and opioid withdrawal in patients with OUDs. Suvorexant is an orexin-1 antagonist that is approved by the FDA for treatment of insomnia because it improves sleep architecture without producing drug dependence. In addition, the orexin system has been involved in the pathophysiology of OUD. Therefore, suvorexant is promising medication to treat the sleep problems of OUD and OUD itself.

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2019 Target**	**FY 2019 Achieved**
Scientific Research Outcome 5.15: By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and SUDs and their consequences in underage populations.	Develop an intervention to prevent or reduce alcohol misuse among college age individuals.	Researchers demonstrated the efficacy of interventions involving brief motivational interviewing and a supplemental activity for reducing alcohol misuse among college age individuals.
Scientific Research Outcome 4.15: By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations.	Test a screening and brief alcohol intervention in an underage population.	Researchers tested NIAAA's Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide's two-question screening tool to determine its predictive ability in identifying future risk for alcohol-related problems in an underage population.

Prevention – Scientific Research Outcome-5.15
The FY 2019 target was met. Brief Motivational Interviewing (BMI) is a cost-effective preventive intervention for alcohol misuse that involves providing individualized feedback on drinking behavior and associated risks. Feedback may include goal-setting strategies for cutting back on drinking or reducing risks of harm. Although BMI is considered an effective

intervention for college-age populations, the magnitude of the effect is typically moderate or small. For this reason, researchers have studied the utility of adding additional intervention elements to enhance the effects of BMI on reducing alcohol consumption and resulting harms among college students. NIAAA-supported researchers conducted a two-site randomized controlled clinical trial in a college student population to evaluate BMI efficacy when supplemented by a substance-free activity session or relaxation training session. Outcomes were evaluated up to 16 months after the intervention. Compared to the control condition, BMI combined with either an activity session or relaxation training was associated with reductions in alcohol use and related problems across the 16-month follow-up period. The combined approach resulted in effects greater in magnitude when compared to previous reports of BMI alone. The same research group conducted an analysis of existing data from three randomized controlled trials specifically to examine the effects of BMI with a supplemental intervention on alcohol-induced blackouts in college-age individuals. Their analyses indicated that, compared to a control group, participants who received BMI in conjunction with either a substance-free activity session or relaxation training were less likely to report a blackout up to six months later. Together, these two studies demonstrate the efficacy of BMI supplemented with an additional intervention session for reducing alcohol misuse and related problems, including alcohol-induced blackouts, and suggest that supplemental activities enhance the impact of BMI effects.

Treatment – Scientific Research Outcome-4.15
The FY 2019 target was met. Several studies have demonstrated the utility of NIAAA's youth alcohol screening guide in identifying youth who are at current risk for alcohol-related problems, but no studies had been performed to test whether it can predict risk for future alcohol problems. A multi-site study conducted at 16 pediatric emergency departments by NIAAA-supported researchers evaluated the two-question screening tool's predictive validity for future alcohol use disorder (AUD). They found that the two-question screening tool has acceptable predictive validity with respect to risk for AUD at one, two, and three years after the initial screening. These findings demonstrate that the youth screening guide is effective for identifying current and future risk for alcohol-related problems in youth.

Additionally, in a recent NIAAA-supported study, researchers examined the effects of screening, brief intervention, and referral to treatment (SBIRT) delivered in pediatric primary care settings on health care use and health outcomes over time. The investigators used electronic health data from a randomized clinical trial of adolescents aged 12-18 years that compared SBIRT delivered either by a pediatrician or behavioral health clinician to usual care. They found that patients who received SBIRT had fewer medical and mental health comorbidities, fewer psychiatry visits after one year, and fewer substance use diagnoses, as well as lower outpatient use over three years. These findings suggest that providing SBIRT in primary care may reduce health care use and improve adolescent health.