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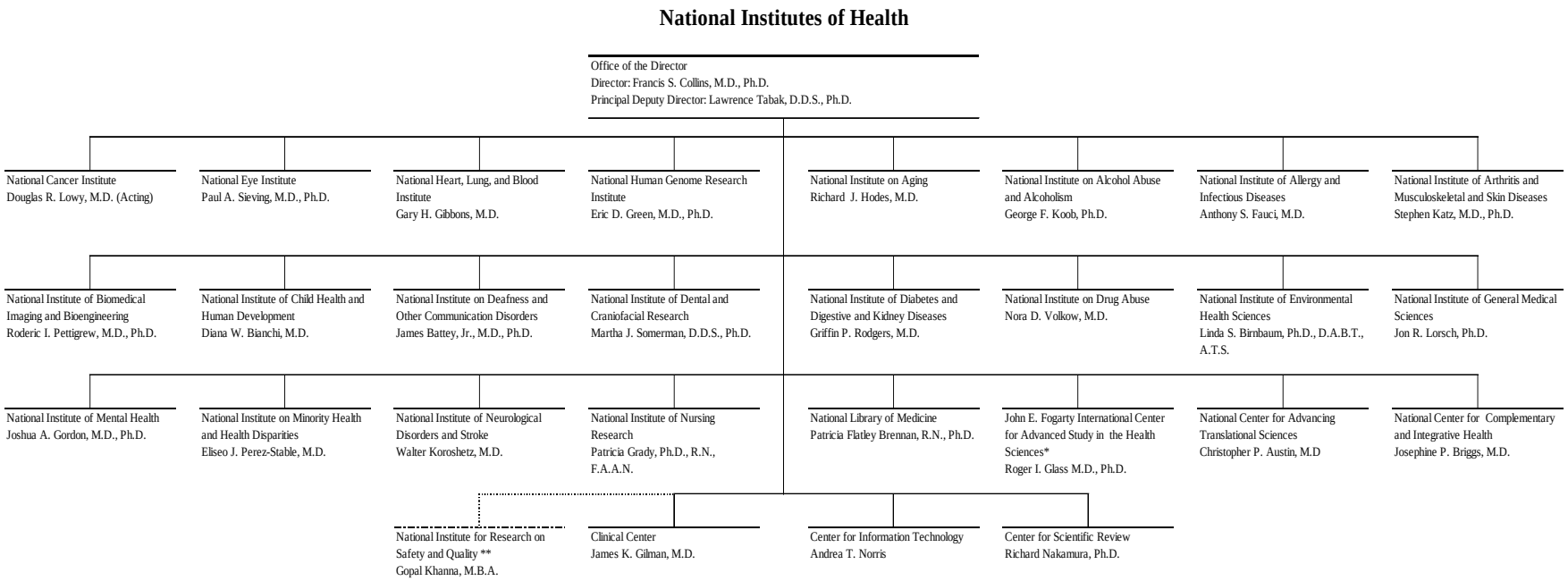

* The FY 2018 Budget proposes to dissolve the Fogarty International Center.
** The FY 2018 Budget proposes to consolidate the Agency for Healthcare Research and Quality into NIH as the National Institute for Research on Safety and Quality.

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 or supports research designed to understand the basic biology of human health and disease; apply this understanding towards designing new approaches for preventing, diagnosing, and treating disease and disability; and ensure that these new approaches are available to all.

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

OVERVIEW OF BUDGET REQUEST

Introduction

For FY 2018, NIH requests a total program level of $26.9 billion, which is -$5.7 billion below the FY 2017 Continuing Resolution level. As announced in the President's Budget Blueprint, a major reorganization of NIH's Institutes and Centers is proposed. The FY 2018 Budget eliminates the Fogarty International Center, while retaining certain mission-critical international research and research-related activities. Approximately $25 million within the Office of the Director will be dedicated to coordinating global health research across the NIH, including issues regarding workforce development and engagement with NIH's international biomedical research partners. The FY 2018 Budget also consolidates the activities of the Agency for Healthcare Research and Quality (AHRQ) within NIH as the National Institute for Research on Safety and Quality (NIRSQ). The Budget includes $272 million in budget authority for NIRSQ, to preserve key activities to improve the quality and safety of American health care while reducing or eliminating lower priority programs that may potentially overlap with activities administered by other components of HHS. These continued activities include critical survey activities, evidence-based practice centers, research to enhance patient safety and health services, and researcher training grants. In addition, NIRSQ is projected to receive $107 million in mandatory resources from the Patient-Centered Outcomes Research Trust Fund to continue the targeted dissemination of study results and workforce development efforts in research designed to help patients and providers make better informed health care decisions. Other reorganization activities proposed for FY 2018 include moving the *All of Us* Research Program out of the Common Fund (but remaining in the Office of the Director), and moving the Science Education Partnership Award program from the Office of the Director to the National Institute of General Medical Sciences.

In FY 2017, Congress enacted the 21st Century Cures Act, authorizing $4.8 billion over ten years in support of high priority NIH initiatives and research areas: the Precision Medicine Initiative's *All of Us* Research Program, the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, the Beau Biden Cancer Moonshot, and Regenerative Medicine. Initial funding of $352 million was appropriated in the Further Continuing and Security Assistance Appropriations Act, 2017. The FY 2018 Budget includes the full $496 million authorized for these initiatives, requested in the new NIH Innovation Account managed by the Office of the Director. The funding for the Cancer Moonshot ($300 million) is to be transferred to the National Cancer Institute; the funding for the BRAIN Initiative is to be transferred to the National Institute of Neurological Disorders and Stroke ($43 million) and the National Institute of Mental Health ($43 million). The remaining funding is $100 million for the *All of Us* Research Program and $10 million for Regenerative Medicine.

Increasing efficiencies within the NIH remains a priority of the Administration. The FY 2018 Budget includes an indirect cost rate for NIH grants that will be capped at 10% of total cost (currently NIH expends approximately 28% of its extramural budget on indirect costs). This approach would be applied to all types of grants with a rate higher than 10 percent. Other entities, including private foundations and payers, spend a much higher portion of their grants on direct science. The current indirect rate setting process requires each grantee to provide hundreds of pages of documentation to negotiate their indirect rate with the government. The

reform approach will release grantees from the costly and time-consuming indirect rate setting process and reporting requirements. The approach will also seek to develop a uniform indirect cost rate to all grants that mitigates the risk for fraud and abuse by simplifying and uniformly applying the rate for grantees.

To continue in the pursuit of cutting-edge advances at the frontier of biomedical research, in FY 2018, NIH will focus on the following priority themes:

1. Fundamental Science Enhanced by Technological Advances
2. Treatments and Cures
3. Health Promotion and Disease Prevention
4. Enhancing Stewardship

By using these themes to guide strategic investments, NIH will continue to drive biomedical discovery and innovation in the United States, maintain the country's competitive edge as a global leader in research, bolster the U.S. economy, and ultimately make significant inroads in improving the health of the Nation.

Theme 1: Fundamental Science Enhanced by Technological Advances

Key to the achievement of its mission is NIH's investment in the essential building blocks of science, which can be applied across NIH's disease portfolio. This includes basic science (knowledge of the mechanisms of biology and behavior), data science, and the development of new technologies. NIH-funded basic science provides the foundation for translational and clinical studies that can lead to major medical advances, such as cancer-fighting drugs, vaccines, and medical devices, as illustrated by case studies of research impact.[1]

In March 2016, the NIH Director, along with several senior agency leaders, penned a letter in the leading biomedical journal *Science* to reaffirm NIH's deep commitment to basic science, stating "that many of the most important medical advances trace back to basic research that had no explicit disease link."[2] Because the private sector funds a limited amount of basic research, NIH's support of fundamental science is vital to the whole U.S. biomedical research enterprise. Basic research continues to represent more than half of NIH's research budget,[3] and provides a substantial return on investment. This investment drives progress along the entire research continuum, ultimately resulting in improved health.

The BRAIN Initiative

The Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative – which includes ten NIH Institutes and Centers (ICs), multiple Federal agencies, and several private partners – continues to support basic neuroscience research aimed at accelerating the development of innovative technologies for understanding the brain. New, cutting edge tools

[1] https://www.nih.gov/about-nih/what-we-do/impact-nih-research/our-stories.
[2] http://science.sciencemag.org/content/351/6280/1405.1.full.
[3] https://officeofbudget.od.nih.gov/pdfs/FY15/Basic%20and%20Applied%20FY%202002%20-%20FY%202015%20%28Transmit%29.pdf.

help scientists better understand not only how intricate networks of brain cells enable us to think, act, and perceive, but also how changes in these networks lead to neurological disease and impairment. A variety of high-impact research is supported by the BRAIN Initiative, including developing tools that can visualize and alter neural activity, creating a molecular census of the myriad cell types in the brain, understanding how and why brain cells connect to one another, and designing better electrodes that can therapeutically stimulate the human brain. FY 2018 funds will continue to support basic neuroscience research, human neuroscience research, scientific training, collaborative activities with other Federal agencies, and partnerships with industry to develop and test novel neurotechnologies, all with the aim of increasing our understanding of the brain and uncovering new ways to treat, cure, or prevent brain disorders.

Single Cell Analysis: Understanding Individual Cells Within a Group

Individual cells within a cluster of the same "type," such as neurons or nephrons, are not identical. In fact, they can differ dramatically and may change rapidly in response to stimuli in their environment. This has important consequences for the health and function of the entire organism. Understanding more about how single cells function could help researchers identify rare cells in a group (e.g., ones that could become cancerous), cells infected latently with a virus, or cells that develop drug resistance. NIH supports the development of game-changing technologies to analyze the dynamic states of single cells. Researchers supported by the NIH Common Fund's Single Cell Analysis Program (SCAP) used single cell analysis to reveal a huge diversity of neuronal subtypes within the human brain.[4] The SCAP Single Cell Analysis Challenge reached out to a diverse array of researchers to develop new tools and methods to measure single cell changes within a complex tissue environment in order to elucidate any functional changes that might affect the health status of the cell. Finalists from Phase 1 took their theoretical ideas into practical applications in the lab for Phase 2. The winners of Phase 2 will be announced in July 2017. Supporting single cell analysis has the potential to uncover fundamental biological principles and ultimately improve the detection and treatment of diseases.

Advances in Microscopy for Enhanced Drug Development

Advances in imaging techniques are providing a window to observe molecular interactions in extraordinary detail. For example, researchers at NIH's National Cancer Institute (NCI) are using cryo-electron microscopy (cryo-EM)—the 2015 scientific method of the year by *Nature Methods*—to view a key protein in cancer cells at a nearly atomic level.[5] Cryo-EM enables researchers to see molecules in a relatively natural state by flash-freezing a sample and bombarding it with electrons to produce images that can be captured with a special type of camera. Although there has been tremendous progress in this technology, it is still far from reaching its full potential, and NIH is supporting efforts to try to achieve that goal. For instance, one recent recipient of an NIH Director's Early Independence Award, a high-risk, high-reward funding mechanism, is developing new cryo-EM techniques to model the atomic structures of proteins much smaller than currently can be imaged. Cryo-EM advances should aid the

[4] Lake BB, et al. *Science* 2016;352(6293):1586-90. PMID:27339989. http://www.ncbi.nlm.nih.gov/pubmed/27339989

[5] Banerjee S, et al. *Science* 2016;351(6275):871-5. PMID: 26822609. http://www.ncbi.nlm.nih.gov/pubmed/26822609

development of more effective treatments, as determining accurate protein structures is key to designing more targeted and effective drugs.

Theme 2: Treatments and Cures

Thanks to fundamental research, we are in the midst of a paradigm shift in medicine – one that seeks to understand the roots of disease and impairment at their most elemental, molecular levels. NIH is investing in technologies that allow researchers and practitioners to screen rapidly for small but meaningful markers in a patient's molecular profile. One thing that is increasingly clear is that many seemingly disparate diseases have commonalities at the molecular level. Not only does this insight allow for new understanding of mechanisms that cause disease, but it also provides opportunities to repurpose existing drugs for use in other conditions. For example, as a result of a public-private partnership, an experimental drug originally developed to fight cancer is now being tested for Alzheimer's disease in human clinical trials. Scientists realized that the way the drug worked in cancer cells might also target a protein that plays a role in how brain cells are damaged in Alzheimer's disease.

Designing effective treatments and cures depends upon innovative, creative researchers translating fundamental knowledge about cells, systems, and organisms, into models for therapeutic development. Cell or tissue samples, animal models, and computer simulations often are used to design and test candidate approaches for diagnostics, devices, treatments, and cures. The most promising are then moved into human clinical trials, where they are tested for safety and efficacy. It is through this innovation pipeline that NIH aims to continue pushing the boundaries of what is possible in modern medicine.

Promising Advances for Sickle Cell Disease

Several NIH-supported researchers are applying a novel method, derived from basic science research, to develop possible treatment options for myriad diseases. The method, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), can alter DNA precisely to correct disease-causing mutations. One group of researchers is applying this method to "fix" the mutations that cause sickle cell disease (SCD). SCD affects as many as 100,000 people in the U.S., and about 1 of every 13 African Americans carries the sickle cell trait. In *in vitro* experiments, these scientists corrected the disease-causing mutation in cells that then went on to produce new red blood cells with healthy hemoglobin. Although the mutation was not fixed in all cells, the frequency was high enough that this result, in addition to studies in mice by the same researchers, indicates that this method could yield an effective treatment for this debilitating disease. While much more research is needed before this approach is ready for human clinical trials, NIH support for developing cutting-edge techniques that can be applied to find new treatments and cures in studies such as this could be a revolutionary approach for drastically improving human health.

Intervening in the Opioid Epidemic

The Nation is in the grips of a public health crisis due to an opioid epidemic. In 2015, a record number of Americans – more than 33,000 – died from overdosing on opioid drugs. These drugs

include prescription pain relievers as well as heroin and illicitly manufactured synthetic opioids such as fentanyl – an opioid that is 80 times more potent than morphine.[6] Addressing this crisis continues to be a high priority across the Department of Health and Human Services (HHS), and NIH is working closely with our partner federal agencies to address the complex problems of prescription opioid misuse and illicit opioid use. NIH supports research efforts focused on: preventing opioid misuse and addiction; developing new and improved treatments for opioid addiction; improving the deployment of evidence based strategies for combatting overdose and preventing and treating addiction; and developing more effective treatments for pain with reduced potential for addiction and misuse, as underscored by the HHS National Pain Strategy, released in March 2016.[7]

With FY 2018 funds, NIH intends to leverage recent scientific advances to combat opioid addiction and overdoses. For example, National Institute on Drug Abuse (NIDA)-supported research contributed to the development of Probuphine©, an implantable formulation of buprenorphine (an opioid used to treat opioid addiction) that delivers a constant dose for six months, which can improve treatment compliance and outcomes. NIDA and several other ICs also will continue their multi-pronged research and dissemination strategy, which may include development and deployment of new formulations of naloxone designed to combat fentanyl overdoses; large-scale epidemiological studies to understand evolving patterns of opioid misuse in hard-hit communities; testing of strategies to improve implementation of preventive interventions; clinical trials on new pharmacological and non-pharmacological interventions (e.g., vaccines and transcranial magnetic stimulation) for opioid addiction; development of alternative pain treatment strategies; and educational and outreach initiatives geared towards multiple audiences, including prescribing physicians and the public.

Combating Antimicrobial Resistance

Though antimicrobial drugs have been used successfully to treat infectious diseases for decades, at least 2 million people in the United States become infected with resistant bacteria annually, leading to 23,000 deaths each year. To address this growing problem, NIH supports the Antibacterial Resistance Leadership Group, which has established a robust program to: perform clinical studies to optimize currently licensed drugs; test diagnostics; and examine best practices in infection control programs and stewardship. NIH also participates in a national, multi-agency effort focused on advancing antimicrobial resistance research, as outlined in the National Action Plan for Combating Antibiotic-Resistant Bacteria.[8] In one effort, NIH is co-sponsoring a monetary prize competition with the HHS Biodefense Advanced Research and Development Authority (BARDA).[9] This prize competition is geared towards developing rapid, point-of-care diagnostics that may be used by healthcare providers to identify bacterial infections, improve treatment of drug-resistant infections, and facilitate antibiotic prescribing and monitoring.[10] NIH

[6] http://www.cdc.gov/media/releases/2015/p1218-drug-overdose.html
[7] https://iprcc.nih.gov/docs/HHSNational_Pain_Strategy.pdf
[8] https://obamawhitehouse.archives.gov/sites/default/files/docs/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf
[9] https://www.challenge.gov/challenge/antimicrobial-resistance-rapid-point-of-care-diagnostic-letter-of-intent/
[10] https://www.nih.gov/news-events/news-releases/antimicrobial-resistance-diagnostic-challenge-selects-10-semifinalists-first-phase-competition

sought public input to help identify the desired characteristics for the diagnostics.[11,12] To support other innovative research, including new classes of antibiotics and non-traditional therapeutic options, NIH's National Institute of Allergy and Infectious Diseases (NIAID) is collaborating with BARDA and others on the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), a new global public-private partnership to advance high-quality antibacterial products into human testing. NIAID will provide in-kind preclinical research support and technical expertise to CARB-X awardees.

Cancer Immunotherapy

The immune system's natural capacity to detect and destroy abnormal cells may be able to prevent the development of many cancers, but this ability often is compromised by cancer cells that avoid detection and destruction by the immune system. However, researchers have developed a powerful new technique to harness a patient's own immune system to attack the cancer cells. This technique, commonly referred to as immunotherapy, is showing great promise. Patients with a variety of cancers, including melanoma, non-small cell lung, chronic lymphocytic leukemia, acute lympoblastic leukemia, colorectal, and breast cancers, already have benefitted from immunotherapy. This rapidly advancing field, based on basic research on the immune system, has produced several new methods of treating cancer. For example, NIH researchers recently created a way to target the cancer-causing protein produced by a mutant form of the gene that causes most pancreatic and many colorectal cancers. This targeted immunotherapy led to cancer regression in the single patient tested in a proof-of-principle study.[13] Additional research is needed to validate this promising method and evaluate its effectiveness in other patients. Another NIH-funded study identified a cell surface receptor that is present on breast, colon, and lung cancer cells. Treatment with an antibody directed to this receptor prevented metastasis in a mouse model of lung cancer, suggesting that this may be a promising treatment for human cancer.[14]

Collectively, the early successes of cancer immunotherapy led the Blue Ribbon Panel (BRP) that is providing scientific direction for the Cancer Moonshot[SM] to recommend creating a translational science network devoted exclusively to immunotherapy. The goal of this network is to develop and implement a national strategy to discover new immune targets and to evaluate new immune-based approaches.[15] In addition to considering the BRP recommendation, ongoing and future NIH-supported research aims to understand what enables immunotherapy to work in some patients, but not in others, as well as to expand the use of immunotherapy to other types of cancer. Studies also will test cancer immunotherapies earlier in disease progression as well as in combination with other standard cancer treatments.

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[11] https://www.federalregister.gov/articles/2015/09/09/2015-22690/announcement-of-public-consultation-on-antimicrobial-resistance-rapid-point-of-care-diagnostic-test
[12] https://dpcpsi.nih.gov/news/AMRpublicforum
[13] Tran E, et al. *N Engl J Med.* 2016; 375(23):2255-2262. https://www.ncbi.nlm.nih.gov/pubmed/27959684
[14] Metelli A, et al. *Cancer Research*. 2016; 76(24):7106-7117. https://www.ncbi.nlm.nih.gov/pubmed/27913437
[15] https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel/blue-ribbon-panel-report-summary.pdf

Theme 3: Health Promotion and Disease Prevention

NIH supports research to promote health, prevent disease, and develop strategies to address the progression of disease before symptoms appear. Advances in these research areas require a deep understanding of the many factors that affect health, and include identification and assessment of genetic and environmental risk factors, screening of at-risk individuals for diseases, development of risk reduction strategies, as well as translation, dissemination, and implementation of strategies to prevent conditions. NIH regularly collaborates with other Departmental agencies to support health promotion and disease prevention activities. A notable example is the coordination between NIH and the Centers for Disease Control and Prevention (CDC) on Ebola virus disease surveillance and clinical trials of candidate Ebola vaccines in West Africa.[16]

All of Us Research Program

Precision medicine aims to develop tools that accurately will tailor medical treatment to an individual patient, a revolutionary approach to disease treatment and understanding of human health. Toward this goal, NIH is establishing a group of one million or more volunteer participants that reflect the diversity of the United States to contribute health information over many years, known collectively as the *All of Us*[SM] Research Program. This cohort will leverage advances in lab technologies, including genomics, computing and data analytics, and adoption of electronic health records, as well as capitalize on mobile health technology that uses smart phones to track health and fitness. In FY 2016, NIH announced awards totaling $55 million to build important partnerships and infrastructure for the *All of Us* program, including a Data and Research Support Center, a Participant Technologies Center, and a network of participating healthcare provider organizations, which includes Federally Qualified Health Centers. The valuable data from this study will help uncover new information about the relationships between a person's environment, genes, and lifestyle. This information can be used to find new strategies for preventing illness as well as effective treatments that account for individual variability, with the eventual goal to improve health and reduce health disparities.

Preventing Public Health Threats Through Vaccine Research

Vaccines represent the safest, most cost-effective, and efficient way to reduce the burden of infectious diseases by preventing them altogether. Creating a safe and effective vaccine often requires understanding how a particular virus or bacteria infects the human body, as well as the various molecules that the immune system might use to target it, requiring a multi-pronged research approach. NIH engages in vaccine research to prevent many diseases, including both emerging threats and recurring maladies.

NIH is at the forefront of efforts to design and test a vaccine to protect against Zika virus infection. The public health threat related to this virus heightened in 2015 and continues to grow. Although the Zika virus is transmitted to humans primarily through mosquitoes, it also can be passed from one person to another through sexual contact, blood transfusion, or from mother to child. The illness caused by this virus is generally mild in adults, but Zika virus

[16] http://www.niaid.nih.gov/topics/ebolamarburg/research/pages/default.aspx

infection can sometimes cause serious birth defects if a mother is infected during pregnancy. NIH's research priorities to combat Zika virus infection include efforts to understand the virus and disease as well as to develop diagnostics, treatments, and vaccines. Several vaccine candidates currently are being developed using different approaches,[17] and NIH's National Institute of Allergy and Infectious Diseases (NIAID) launched the first clinical trial to test the safety and efficacy of one vaccine candidate in August 2016. Early results indicate that the vaccine is safe and that it induces an antibody response against Zika virus. With these promising indicators, a Phase 2/2b clinical trial of the vaccine began in March 2017 to obtain additional safety and immune response data in humans as well as to gauge whether the vaccine protects against disease caused by natural Zika infection.[18]

NIH also is engaged in efforts to develop a "universal" influenza vaccine to protect against the seasonal infection that can sometimes lead to serious health complications. While a new influenza vaccine is released every year, this vaccine currently is created by selecting the most likely strains of virus for a given year months in advance of the flu season, which can result in a less effective vaccine if the predominant strain is not included. In addition, many molecular components of the flu virus mutate rapidly, and so the molecules used to create a vaccine one year may not be effective in future years. Thus, NIH-supported research seeks to develop a "universal" influenza vaccine that induces a potent, durable immune response to conserved elements of the influenza virus that undergo few changes from season to season and strain to strain. Several NIH-funded researchers have made progress towards this goal by targeting a particular protein on the surface of the virus, several versions of which are being evaluated for further clinical study. In addition, Phase 1/2 clinical trials already are underway for an alternative approach involving a DNA-based vaccine and a seasonal booster.

Theme 4: Enhancing Stewardship

As stewards of Federal investments in biomedical research, it is essential that NIH earns and maintains the public's trust. The role of the United States as a leader in biomedical research depends not only on innovation in the laboratory and the clinic, but also innovation in how science is funded, performed, managed, and regulated. NIH is committed to being an efficient and effective steward of taxpayer funds and to encouraging good stewardship practices across all levels of the biomedical research enterprise. NIH strives to allocate its resources with sufficient transparency to allow taxpayers to see how their money is invested. For example, starting in 2017, NIH IC will make information about each IC's funding decisions for each fiscal year more publically available. In coordination with other scientific agencies, NIH continually looks to streamline administrative processes that can take investigators' time away from their research, and is engaged in efforts to make sure that the research conducted with NIH funds is of the highest quality. Most importantly, NIH invests in the long-term health of the Nation by strengthening and sustaining a diverse, world-class research workforce. These efforts ensure that NIH not only funds the best science, but also effectively manages both the present and future of the nation's biomedical research enterprise.

Increasing the Rigor and Reproducibility of NIH Research

[17] https://www.niaid.nih.gov/diseases-conditions/zika-vaccines
[18] https://www.nih.gov/news-events/news-releases/phase-2-zika-vaccine-trial-begins-us-central-south-america

One of the key ways in which NIH is enhancing stewardship is through the promotion of rigorous, unbiased biomedical research. To continue to support this goal, NIH recently released and implemented a policy to enhance reproducibility through increased scientific rigor and transparency in reporting.[19] In addition to the new policy, NIH released principles and guidelines for reporting preclinical research and created training materials for graduate students and fellows. Planned future activities include extending the previously established Rigor and Reproducibility Policy to institutional training grants and fellowships, collaborating with scientific journal editors to improve rigor and reproducibility in publications, and working to improve data sharing and accessibility. NIH also has engaged the Advisory Committee to the Director of NIH to make recommendations, informed by existing activities, to enhance rigor and reproducibility of scientific research funded by NIH. These approaches are designed to strengthen a culture that encourages best practices for rigorous scientific research and reporting.

Supporting New Investigators

Excellence in biomedical research depends upon cultivating a world-class biomedical research workforce – one that is diverse, creative, innovative, and productive. NIH works to make sure that the next generation of scientists thrives, including those from underrepresented groups. To ensure fairness in the funding process, NIH has created procedures to normalize success rates between early and more experienced investigators. In addition, a number of funding opportunities directly target new and early stage investigators, including programs that allow exceptional individuals to skip the traditional postdoctoral training period or that provide support to bridge the gap from early to mid-career stages. Another of these high risk, high reward programs is the NIH Director's New Innovator Award, which supports remarkably creative new investigators with groundbreaking, novel research ideas at an early stage of their career. With an emphasis on innovation and originality, preliminary data are not needed for this award. Following these models, several ICs also have specialized award programs to support investigators during early career stages. In addition to supporting specific grant policies and awards, programs like the Early Career Review Program provide young investigators with an invaluable opportunity to participate in NIH's peer review process and to understand better how to generate a successful grant application. In FY 2018, NIH will use the Next Generation Researchers Initiative, established by the 21st Century Cures Act, to further address how best to support new investigators. This initiative aims to coordinate policies and programs at NIH that provide opportunities for new researchers and could lead to earlier research independence.

Conclusion

NIH funds rigorous science that expands our understanding of living systems and drives improvements in health. The programs, activities, and investments described here illustrate NIH's strategic vision for biomedical research, one that capitalizes on new opportunities for scientific exploration and addresses major challenges for human health. This process was exemplified in FY 2016 when NIH released a centralized NIH-Wide Strategic Plan. While each of NIH's component Institutes, Centers, and Offices routinely publishes strategic plans that align with their congressionally mandated missions, the NIH-Wide Strategic Plan coalesces the goals

[19] https://grants.nih.gov/reproducibility/index.htm

of the agency and harmonizes decision-making across the agency. The Plan emphasizes NIH's commitment to advancing opportunities in the full range of biomedical research, while ensuring that it makes smart, well-managed investments as stewards of taxpayer funds. From setting careful priorities, to cultivating the research workforce of the future, to developing and applying the tools NIH needs to understand the content and results of its research portfolio, NIH strives to capitalize on the most promising opportunities and combat the most pressing challenges facing society today.

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 2018 budget request reflects the Agency's longstanding commitment to invest strategically using performance-based analysis, as emphasized in the GPRA Modernization Act of 2010 (P.L. 111-352). Through the continuous evaluation and strategic management of its research portfolio, NIH focuses on funding research that shows the greatest promise for improving the overall health of the American people. In addition, NIH continually seeks to identify and address high-priority scientific opportunities and emerging public health needs. By managing its research portfolio to support key research priorities, NIH ensures the most effective use of funds to achieve the greatest impact on the health and welfare of the Nation. In particular, NIH's strong peer-review process, site visits, performance monitoring, program evaluation, and performance-based contracting enable the Agency to ensure that its investments generate results for the American people.

NIH strives to achieve transparency and accountability by regularly reporting results, achievements, and the impact of its activities. To increase transparency and promote effective use of resources, NIH began reporting the amount of indirect costs paid per grant on its Research Portfolio Online Reporting Tools website (NIH RePORT) in October 2013. NIH supports a wide spectrum of biomedical and behavioral research and engages in a full range of activities that enable research, its management, and the communication of research results. Because of this diversity and complexity, NIH uses a set of performance measures that is representative of its activities and is useful for tracking progress in achieving performance priorities. This representative approach has helped NIH to share progress of its performance priorities with HHS, the rest of the Executive Branch, the Congress, and the public.

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. The measures also support the Administration's goal of protecting and improving the health and well-being of the American people.

Performance Management

Performance management at NIH is an integrated and collaborative process to ensure that the Agency is achieving its mission to conduct and support research to improve public health. At the Agency level, the NIH Director sets priorities, monitors performance, and reviews results across the 27 ICs and OD. OD is the central office responsible for setting policy for NIH, and for planning, managing, and coordinating the programs and activities of all NIH components. The NIH Director provides leadership to the ICs and helps identify needs and opportunities, especially for efforts that involve multiple ICs. Each IC and OD office carries out priority setting, performance monitoring, progress reviews, and makes adjustments based on progress achieved in their respective areas of science. In addition to the performance management processes that occur for the NIH research program, there are equivalent processes for administrative management functions.

The NIH performance framework includes: 1) priority setting with input from key stakeholders; 2) implementation and management of activities that support priorities; 3) monitoring and assessment of progress, and identification of successes and challenges; 4) oversight by IC leadership and OD office directors in assessing overall progress toward priorities and identification of best practices, appropriate next steps, and corrective actions (as needed); 5) incorporation of regular feedback from IC and OD office leadership to enhance activities; 6) regular reviews of priorities, progress, and outcomes by the NIH Director and IC Directors; and 7) regular review of performance and priorities by external expert review groups including grant peer-review groups, Advisory Councils, and ad hoc working groups.

Qualitative and quantitative information is used to monitor progress and help to identify successes, as well as obstacles in achieving short and long-term goals. Supporting high-performing research is a process of adapting to new developments or newly identified barriers, or shifting resources to pursue promising unanticipated results that may provide critical new information. Moreover, the impact of research may not be immediately known and may depend on additional development or on advances in other fields. Despite these challenges, NIH leadership is able to manage performance effectively by using the best available information to assess progress toward achieving priorities and making appropriate adjustments.

Research is an inherently collaborative endeavor, and partnerships are crucial to achieving scientific research outcomes. The role of the extramural research community (the scientists at universities and hospitals across the country and around the world) as NIH's partner in research is well known. However, of increasing importance are partnerships with private companies, not-for-profit institutions, non-governmental organizations, other Federal agencies, and state and international entities. Joint research and training activities and other exchanges with such groups increase the leverage of NIH resources and support vibrant partnerships to help NIH achieve its mission. Moreover, such partnerships facilitate valuable information feedback loops that identify emerging needs, suggest important new research questions, and otherwise inform priority setting. Partnerships also provide access to populations that are essential to advancing knowledge.

All scientific research carried out through NIH support is subjected to a rigorous and consistently applied review process. For example, the Extramural Research Program, which includes the largest category of NIH-funded research, utilizes two levels of peer review. The first level consists of chartered scientific review groups composed of outside experts in particular scientific disciplines. The second level is the National Advisory Councils of the ICs. For the Intramural Research Program, the progress of individual scientists and their laboratories is evaluated once every four years by Boards of Scientific Counselors composed of external experts. These reviews enable ongoing assessments of all intramural labs and the accomplishments of the scientists who contribute to them. It is through this well-honed system of peer review that NIH maintains its focus on supporting research of the highest possible quality.

The NIH approach to performance management is undergirded by the NIH Governance Structure. That structure includes the NIH Steering Committee and seven standing Working Groups.[20, 21] Ad-hoc working groups are established, as needed, to address emerging issues. The premise of the structure is that shared governance, which depends on the active participation of the IC Directors with the NIH Director, will foster the collaborative identification of corporate issues and a transparent decision-making process. With active participation by the IC Directors in NIH-wide governance, NIH can maximize its perspective and expertise in the development and oversight of policies common to NIH and its ICs. Through the governance process, corporate decisions are made; these may be long-term and strategic (e.g., facilities planning, budget strategy, research policy direction) or short-term and tactical (e.g., stipend levels, resource allocations and compliance oversight). This process does not include issues related to the setting of scientific priorities, which is reserved for meetings of all IC Directors. The NIH Director meets with the IC Directors on a bi-weekly basis, and scientific initiatives are discussed, as well as major management issues that affect the Agency. In addition, scientists – from within and outside the Agency – are invited to present on new or emerging research opportunities. The NIH Director stays informed of priorities through regular meetings with IC and OD Office Directors. Similarly, the IC Directors monitor performance through regular meetings with the Division Directors and Scientific/Clinical Directors in their respective ICs.

Based on these reviews, leadership and their staff take appropriate actions to support research activities. For example, the reviews may lead to the development of new award programs for early-career researchers, the development of new funding announcements for promising research areas, or new collaborations across NIH and/or with other Federal and non-Federal partners. The NIH Director and senior leadership receive regular updates on the progress of the priorities, provide feedback, and incorporate the latest information into the NIH's overall planning and management efforts. This constant feedback loop enables NIH to make critical adjustments periodically to align activities and target resources in support of its research priorities.

[20] The NIH Steering Committee is composed of the NIH Director, Deputy Director (ex-officio), the Directors of NCI, NHLBI, and NIAID, as well as a balance of Directors from the smaller and medium-sized institutes.
[21] The seven standing working groups are: Extramural Activities, Diversity, Facilities, Management and Budget, Scientific Data Council, Administrative Data Council, and Clinical Center Governing Board.

ALL PURPOSE TABLE

All Purpose Table[1]
(Dollars in Thousands)

(Dollars in Thousands)[1]	FY 2016 Final	FY 2017 Annualized CR[2]	FY 2018 President's Budget[2,3]	FY 2018 President's Budget +/- FY 2017 Annualized CR
Total, NIH Program Level	**$32,311,349**	**$32,593,341**	**$26,919,710**	**-$5,673,631**
Less mandatory and funds allocated from different sources:				
Mandatory Type 1 Diabetes Research	150,000	139,650	150,000	10,350
PHS Program Evaluation	780,000	780,000	780,000	0
Patient-Centered Outcomes Research Trust Fund	NA	NA	106,546	NA
Total, NIH Discretionary Budget Authority	**$31,381,349**	**$31,673,691**	**$25,883,164**	**-$5,790,527**
Interior Budget Authority	77,349	77,202	59,607	-17,595
Total, NIH Labor/HHS Budget Authority	**$31,304,000**	**$31,596,489**	**$25,823,557**	**-$5,772,932**
Number of Competing RPGs	*10,364*	*8,974*	*7,326*	*-1,648*
Total Number of RPGs	*35,580*	*35,349*	*33,403*	*-1,946*
FTEs	*17,723*	*18,105*	*18,365*	*260*

[1] Excludes Ebola-related and Zika-related supplemental appropriations.

[2] Includes 21st Century Cures Act funding.

[3] Includes funding and FTE for the National Institute for Research on Safety and Quality; does not include funding for the Fogarty International Center

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	**FY 2017 Annualized CR**	**FY 2018 President's Budget**	**FY 2018 +/- FY 2017**
Research Project Grants	$17,927.331	$14,188.712	-20.9%
Competing Average Cost (in thousands)	$484.800	$389.436	-19.7%
Number of Competing Awards (whole number)	8,974	7,326	-18.4%
Estimated Competing RPG Success Rate (absolute rate)	17.1%	13.7%	-19.9%
Research Centers	$2,496.279	$2,079.715	-16.7%
Other Research	$2,151.400	$1,731.883	-19.5%
Training	$843.291	$737.508	-12.5%
Research & Development Contracts	$2,911.704	$2,489.201	-14.5%
Intramural Research	$3,672.888	$3,064.128	-16.6%
Research Management and Support	$1,718.144	$1,576.596	-8.2%
Common Fund (non-add)	$674.355	$454.423	*-32.6%*
Buildings & Facilities Appropriation	$128.618	$98.615	-23.3%
Other Mechanisms[1]	$743.687	$953.352	28.2%
Total, Program Level[2]	**$32,593.342**	**$26,919.710**	**-17.4%**

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

[2] Includes discretionary budget authority received from Labor/HHS appropriations (ICs) and the Interior appropriation (Superfund). Also includes mandatory budget authority derived from the Special Type 1 Diabetes account and Patient-Centered Outcomes Research Trust Fund (PCORTF), and Program Evaluation Financing.

BUDGET BY HHS STRATEGIC OBJECTIVE

National Institutes of Health
FY 2018 Budget by HHS Strategic Objective
(Dollars in Millions)

(Dollars in Millions)	FY 2017 Annualized CR
1.Strengthen Health Care	
1.A Make coverage more secure for those who have insurance, and extend affordable coverage to the uninsured	
1.B Improve health care quality and patient safety	
1.C Emphasize primary and preventive care, linked with community prevention services	
1.D Reduce the growth of health care costs while promoting high-value, effective care	
1.E Ensure access to quality, culturally competent care, including long-term services and supports, for vulnerable populations	
1.F Improve health care and population health through meaningful use of health information technology	
2. Advance Scientific Knowledge and Innovation	**32,448**
2.A Accelerate the process of scientific discovery to improve health	32,448
2.B Foster and apply innovative solutions to health, public health, and human services challenges	
2.C Advance the regulatory sciences to enhance food safety, improve medical product development, and support tobacco regulation	
2.D Increase our understanding of what works in public health and human services practice	
2.E Improve laboratory, surveillance, and epidemiology capacity	
3. Advance the Health, Safety and Well-Being of the American	
3.A Promote the safety, well-being, resilience, and healthy development of children and youth	
3.B Promote economic and social well-being for individuals, families, and communities	
3.C Improve the accessibility and quality of supportive services for people with disabilities and older adults	
3.D Promote prevention and wellness across the life span	
3.E Reduce the occurrence of infectious diseases	
3.F Protect Americans' health and safety during emergencies, and foster resilience to withstand and respond to emergencies	
4. Ensure Efficiency, Transparency, Accountability, and Effectiveness of HHS Programs	**145**
4.A Strengthen program integrity and responsible stewardship by reducing improper payments, fighting fraud, and integrating financial, performance, and risk management	
4.B Enhance access to and use of data to improve HHS programs and to support improvements in the health and well-being of the American people	
4.C Invest in the HHS workforce to help meet America's health and human services needs	
4.D Improve HHS environmental, energy, and economic performance to promote sustainability	145
TOTAL	**32,593**

BUDGET MECHANISM TABLE

(Dollars in Thousands)	FY 2016 Final[1,3]		FY 2017 Annualized CR[1,3,4]		FY 2018 President's Budget[1,4,10]	
	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	23,528	$11,726,633	24,595	$12,535,005	24,499	$10,531,990
Administrative Supplements	*(1,832)*	281,273	*(1,456)*	173,272	*(955)*	100,722
Competing:						
Renewal	1,641	925,443	1,400	755,198	1,108	439,836
New	8,689	4,071,994	7,558	3,589,996	6,204	2,409,846
Supplements	34	21,342	16	5,403	14	3,322
Subtotal, Competing	10,364	$5,018,779	8,974	$4,350,597	7,326	$2,853,005
Subtotal, RPGs	33,892	$17,026,685	33,569	$17,058,875	31,825	$13,485,717
SBIR/STTR	1,689	810,307	1,780	868,456	1,578	702,996
Research Project Grants	35,580	$17,836,992	35,349	$17,927,331	33,403	$14,188,712
Research Centers:						
Specialized/Comprehensive	1,053	$1,812,218	1,044	$1,769,290	1,011	$1,524,921
Clinical Research	67	406,678	67	377,967	67	282,432
Biotechnology	98	179,563	96	173,920	87	132,574
Comparative Medicine	47	120,096	48	118,451	51	100,132
Research Centers in Minority Institutions	23	56,759	27	56,651	18	39,656
Research Centers	1,288	$2,575,314	1,282	$2,496,279	1,234	$2,079,715
Other Research:						
Research Careers	3,618	$642,441	3,626	$666,150	3,554	$591,562
Cancer Education	74	23,261	76	23,261	74	20,901
Cooperative Clinical Research	345	404,684	327	397,967	298	343,564
Biomedical Research Support	107	67,235	109	69,949	112	55,907
Minority Biomedical Research Support	272	105,494	271	104,885	265	93,799
Other	1,855	776,404	2,000	889,189	1,492	626,150
Other Research	6,271	$2,019,519	6,409	$2,151,400	5,795	$1,731,883
Total Research Grants	43,139	$22,431,826	43,040	$22,575,010	40,432	$18,000,310
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs	
Individual Awards	3,282	$148,181	3,445	$160,074	3,076	$136,690
Institutional Awards	12,446	656,284	12,474	683,217	11,203	600,818
Total Research Training	15,728	$804,466	15,919	$843,291	14,279	$737,508
Research & Develop. Contracts	2,716	$2,915,277	2,509	$2,911,704	1,965	$2,489,201
(SBIR/STTR) (non-add)[2]	*(114)*	*(66,841)*	*(118)*	*(71,943)*	*(76)*	*(61,829)*
Intramural Research	6,884	$3,684,875	6,986	$3,672,888	7,009	$3,064,128
Res. Management & Support	5,410	1,653,326	5,762	1,718,144	5,947	1,576,596
Res. Management & Support (SBIR Admin) (non-add)[2]		*(3,427)*		*(6,187)*		*(26,285)*
Office of the Director - Appropriation[2,5]		*(1,570,790)*		*(1,620,212)*		*(1,452,433)*
Office of the Director - Other		599,368		650,485		777,199
ORIP (non-add)[2,5]		*(295,784)*		*(295,373)*		*(220,811)*
Common Fund (non-add)[2,5]		*(675,639)*		*(674,355)*		*(454,423)*
Buildings and Facilities[6]		144,863		144,618		108,615
Appropriation		*(128,863)*		*(128,618)*		*(98,615)*
Type 1 Diabetes[7]		-150,000		-139,650		-150,000
Program Evaluation Financing[8]		-780,000		-780,000		-780,000
Subtotal, Labor/HHS Budget Authority		**$31,304,000**		**$31,596,489**		**$25,823,557**
Interior Appropriation for Superfund Research		77,349		77,202		59,607
Total, NIH Discretionary B.A.		**$31,381,349**		**$31,673,691**		**$25,883,164**
Type 1 Diabetes and PCORTF[9]		150,000		139,650		256,546
Total, NIH Budget Authority		**$31,531,349**		**$31,813,341**		**$26,139,710**
Program Evaluation Financing		780,000		780,000		780,000
Total, Program Level		**$32,311,349**		**$32,593,341**		**$26,919,710**

1 All Subtotal and Total numbers may not add due to rounding.
2 All numbers in italics and brackets are non-add.
3 Excludes Ebola-related and Zika-related supplemental appropriations.
4 Includes 21st Century Cures Act funding.
5 Number of grants and dollars for the Common Fund and ORIP components of OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriations also is noted as a non-add because the remaining funds are accounted for under OD - Other.
6 Includes B&F appropriation and funds for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
7 Number of grants and dollars for mandatory Type I Diabetes are distributed by mechanism above; therefore, Type I Diabetes amount is deducted to provide subtotals only for the Labor/ HHS Budget Authority.
8 Number of grants and dollars for Program Evaluation Financing are distributed by mechanism above; therefore, the amount is deducted to provide subtotals only for the Labor/HHS Budget Authority.
9 Patient-Centered Outcomes Research Trust Fund included in FY 2018.
10 Includes funding for the National Institute for Research on Safety and Quality; does not include funding for the Fogarty International Center.