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 lay the foundation for ensuring the Nation's economic well-being. This role has been more important than ever in the last few years as NIH has contributed to the development of testing, vaccines, treatments, and other measures necessary to face COVID-19, the greatest public health crisis of our generation. NIH also works to develop, maintain, and renew scientific, human, and physical resources that will ensure the Nation's capability to prevent disease and disability. The biomedical research enterprise depends upon not only NIH's support of cutting-edge science and technology, but also its wise investment of tax dollars. Through careful stewardship of public resources in pursuit of its mission, NIH strives to enhance the lives of all Americans.

OVERVIEW OF BUDGET REQUEST

Introduction

For FY 2023, the National Institutes of Health (NIH) requests a total program level of $62.5 billion. This budget level will support 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. The request allows NIH to make bold new strategic investments to address several national priorities, including combatting the acute and lasting effects of the COVID-19 pandemic, fighting the opioid epidemic, eradicating HIV in the United States, expanding mental health research, addressing health disparities and inequities, researching the human health impacts of climate change, contributing to the HHS Pandemic Preparedness Plan, and continuing to fund the newly established Advanced Research Projects Agency for Health (ARPA-H) that was first proposed in the FY 2022 President's Budget.

On July 31, 2021, NIH released the NIH-Wide Strategic Plan for Fiscal Years 2021–2025 to articulate the agency's highest priorities over the next five years and fulfill requirements of the *21st Century Cures Act.*[1] The Plan will guide NIH research investments and outlines the agency's vision for the direction, capacity, and stewardship of biomedical research. It is organized around a *Framework* of three key *Objectives* that outline these priorities along with five *Cross-Cutting Themes* that are common to all *Objectives*. Individual strategic plans of NIH Institutes, Centers, and Offices, designed to address their specific congressionally mandated missions, link to the NIH-Wide Strategic Plan, and conform to the overarching principles it conveys. In developing the Plan, NIH adopted an approach designed to be transparent, focused on science and good stewardship of research, and guided by evidence. It was developed through collaboration between NIH leadership and staff and key stakeholders, including the research community, professional societies, advocacy groups, and the public. NIH research investments will be guided by the NIH-wide Strategic Plan.

The *21st Century Cures Act* provided NIH with critical tools and resources to advance biomedical research across the spectrum, from foundational basic research studies to advanced clinical trials of promising new therapies. The Innovation Fund, established in the *21st Century Cures Act*, continues to support cutting-edge research through several ongoing initiatives: the *All of Us* Research Program, the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, and the Beau Biden Cancer Moonshot. The Budget includes $1,085.0 million from the Innovation Fund for these projects, an increase of $681.0 million from the FY 2022 Continuing Resolution (CR) level for the Innovation Fund component of the Cures program, which will allow Cures programs to continue to make important strides in FY 2023.

> *All of Us*. In FY 2021, the *All of Us* Research Program continued its mission to accelerate health research and medical breakthroughs to enable individualized prevention, treatment, and care. *All of Us* is on its way to enrolling one million or more participants, and as of February 2022, nearly 466,000 participants have consented to join the program and more than 321,000 participants had completed all steps in the initial protocol. More than 20 publications have now used *All of Us* data.

[1] www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2021-2025-508.pdf

NIH BRAIN® Initiative. The BRAIN® Initiative has enabled scientific advances that provide opportunities to understand the structure and function of the brain at an unprecedented level of detail. Researchers throughout neuroscience are rapidly adopting these advances, and the BRAIN Initiative is both dramatically enhancing existing methods and developing entirely new technologies to study and manipulate brain circuits. In October 2021, the BRAIN® Initiative Cell Census Network (BICCN) unveiled an unprecedented atlas of cell types and an anatomical neuronal wiring diagram for the mammalian primary motor cortex, derived from detailed studies of mice, monkeys, and humans.[2] This atlas was created through an international collaborative effort by more than 250 scientists at more than 45 institutions across 3 continents. The BRAIN® Initiative has also taken major steps in shifting the research culture within neuroscience through its emphasis on neuroethics, diversity and inclusion in the research community, and data sharing practices to enable and enhance the scientific and technological advances from this initiative.

The Beau Biden Cancer Moonshot. Remarkable progress and scientific accomplishments in cancer research have been made in the time since the Cancer Moonshot was launched. The initiative was designed to accelerate cancer research, to make more therapies available to more patients, while also improving our ability to prevent cancer and detect it at an early stage.[3] In February 2022, President Biden announced a bold new goal to continue the progress against cancer achieved by the Cancer Moonshot: cutting America's age-adjusted death rate due to cancer by 50 percent over the next 25 years. To achieve this goal, NCI will support a range of compelling priorities that include diagnosing cancer sooner, addressing inequities that lead to disparities in cancer outcomes, and providing comprehensive support to cancer patients, survivors, and caregivers. The Budget includes an increase of $21.0 million for the Cancer Moonshot from the FY 2022 CR level, for a total of $216.0 million. The fight against cancer will also receive an important boost from creation of the recently established ARPA-H, which will drive transformational innovation in a number of health research areas, including cancer. The Moonshot and ARPA-H initiatives have the potential to impact all cancer patients, including the 1.9 million U.S. patients expected to be diagnosed with cancer in 2021, and the nearly 18 million cancer survivors in the United States, fulfilling the President's commitment to end cancer as we know it.

More than 80 percent of NIH's funding is awarded for extramural research, largely through more than 55,000 competitive grants that support the work of more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every state, the District of Columbia, Puerto Rico, and several tribes. In addition, NIH supports 6,000 intramural scientists making the intramural program one of the largest biomedical research organizations in the world. To date, 165 NIH-supported researchers, including 26 intramural investigators, have been awarded the Nobel Prize. The Lasker Prize, which is often called "America's Nobel,"

[2] www.ninds.nih.gov/News-Events/News-and-Press-Releases/Press-Releases/NIH-BRAIN-Initiative-Unveils-Detailed-Atlas

[3] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative

recognizes researchers and clinicians for their contributions to medicine and has been awarded to 195 NIH-supported researchers to date, including 33 intramural investigators.

Throughout the NIH, a critical aspect of supporting the discovery of novel diagnostics, therapeutics, and cures to disease is having facilities that can house state-of-the-art imaging equipment, discover tumors at the earliest stage possible, safely develop novel treatments such as cellular therapy, and more. Facilities must co-evolve with science for NIH to achieve its full potential. A major component of the Building and Facilities (B&F) program is the Repair & Improvement (R&I) program, which enables NIH to maintain and improve the performance of existing facilities throughout their life cycle. As the responsible steward of its 261 facilities, a key aspect of NIH's strategy is to sustain the condition of existing facilities to prevent premature deterioration and the curtailment of research. These investments help reduce the likelihood and consequences of building emergencies associated with NIH's Backlog of Maintenance and Repairs (BMAR), estimated at nearly $3.0 billion across all campuses as of the end of FY 2021. The FY 2023 B&F request is $300.0 million, a $100.0 million increase from the FY 2022 CR level. This funding is critical to avoid falling even further behind in addressing BMAR.

To achieve its priorities in the facilities area, NIH plans to execute various modernization and repair projects to NIH's research hospital, replace research animal facilities with a centralized and more efficient facility, improve facilities that advance computational and data science, replace temporary and obsolete administrative support facilities with permanent buildings, improve the energy and water efficiency of buildings, and support the co-evolution of science and buildings. NIH will pursue these priorities through the proposed increase in the B&F appropriation as well as an expanded ability for Institutes and Centers (ICs) to contribute toward facilities projects. NIH proposes a revision to the Section 216 authority to eliminate the $3.5 million per project limit and add new authority to transfer IC appropriations to the B&F Account, subject to a 1 percent cap. These new flexibilities will allow NIH to take greater advantage of this important authority and use more of its B&F funds for BMAR-reducing projects.

Previous research that laid the groundwork to respond to the pandemic

Investments in basic research that generate fundamental knowledge about the nature and behavior of living systems provide the building blocks that allow us to respond effectively to new challenges. This foundational science includes basic biological, behavioral, and social research that generates the knowledge of how living systems work at the molecular, cellular, organismal, behavioral, and social levels. In pursuit of its mission, NIH invests more than half of its research budget in fundamental discovery, which provides the key for unlocking the secrets of how living systems function.[4] With this substantial level of support, NIH lays the groundwork for discoveries that will ultimately lead to improved health outcomes. In fact, a recent study found that NIH funding contributed to published research associated with every single one of the 210 new drugs approved by the U.S. Food and Drug Administration (FDA) from 2010 through 2016.[5]

[4] nexus.od.nih.gov/all/2016/03/25/nihs-commitment-to-basic-science/
[5] www.pnas.org/content/115/10/2329

From basic research to vaccines
The COVID-19 pandemic has underscored the importance of vaccines for a healthy and prosperous nation. Building on a foundation of research on molecular biology and immunology, as well as specific previous research on Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), NIH scientists and grantees were positioned to rapidly develop COVID-19 vaccine candidates for testing in clinical trials, achieving FDA emergency use authorization in just 11 months – about five times faster than has even been achieved previously for a vaccine. The fundamental research foundations of messenger RNA technologies used in the Pfizer and Moderna COVID-19 vaccines that are currently being deployed to millions of Americans stretch back over 15 years of NIH support.

Building on existing networks to respond to the pandemic
Across the NIH, existing collaborative infrastructure was repurposed to study and respond to the emerging and ongoing pandemic. For example, at the start of the pandemic, *All of Us* was already positioned to aid researchers around the country who were interested in studying the impact of COVID-19.[6] The program's COVID-19 research initiatives included antibody serology testing participant samples, the on-going collection and expansion of electronic health record data available to researchers, and the results of the COVID-19 Participant Experience (COPE) survey in which more than 100,000 participants completed at least one survey. Meanwhile other already established networks, such as the Clinical and Translational Science Awards (CTSA) Trial Innovation Network, have been efficiently coordinating multiple clinical trials during the pandemic in partnership with the NIH Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) efforts. CTSA-supported institutions are currently conducting trials testing therapeutic options for COVID-19, including the use of immunomodulators and repurposing of existing drugs already approved for other uses.

Changes in research to quickly respond to needs associated with the pandemic

The portfolio of NIH-funded research has changed in response to needs associated with the pandemic. Topics that were of high priority to the NIH before the pandemic, such as ending the opioid epidemic and developing a universal influenza vaccine, are now even more urgent. Meanwhile NIH has unfortunately added new diseases to its portfolio, including persistent symptoms after acute SARS-CoV-2 infection, known as Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) or just "Long-COVID."

Addiction and Overdose Crisis
Since early in the pandemic, studies have found increases in the use of many kinds of drugs, including fentanyl, cocaine, heroin, methamphetamine, cannabis, and alcohol. The crisis of opioid misuse, addiction, and overdose in the United States is a rapidly evolving and urgent public health emergency. In 2020, there were over 90,000 drug overdose deaths in the United States.[7] More than 2 million Americans have opioid use disorder (OUD), and 10 million Americans misuse opioids. Additionally, more than 25 million Americans experience daily pain, putting them at increased risks for opioid use and misuse.[8] These staggering numbers are likely

[6] www.joinallofus.org/coronavirus
[7] www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
[8] www.ncbi.nlm.nih.gov/pmc/articles/PMC6688196/pdf/collins-1536332.pdf

underestimated. They fail to capture the full extent of the damage of the opioid crisis, which reaches across every domain of family and community life — from lost productivity and economic opportunity, to intergenerational and childhood trauma, to extreme strain on community resources, including first responders, emergency rooms, hospitals, and treatment centers. In response to this crisis, NIH launched the Helping to End Addiction Long-term® Initiative, or NIH HEAL Initiative, to provide scientific solutions to the opioid crisis and offer new hope for individuals, families, and communities affected by this devastating crisis. This cross-cutting NIH effort spans basic, translational, clinical, and implementation science on opioid misuse, addiction, and pain. HEAL has funded over $2.0 billion in research, representing more than 600 research projects across the United States. These projects aim to identify new therapeutic targets for both pain and opioid use disorder, reduce the risk of opioids through nonpharmacological strategies for pain management, and improve opioid addiction treatment in a variety of settings.

Since the launch of HEAL, COVID-19 has collided with the opioid crisis in profound ways. Since the declaration of a public health emergency for COVID-19, overdoses increased 42 percent in May 2020 compared to May 2019.[9] The COVID-19 pandemic caused significant disruption to pain management and OUD/substance use disorder (SUD) treatment and recovery services. Furthermore, the rise of non-prescribed fentanyl in combination with other drugs requires new approaches to combat overdose in the United States.[10] In order to continue to respond to these evolving challenges, the FY 2023 President's Budget includes total funding of $2,620.8 million to address the opioid crisis across the ICOs, an increase of $626.6 million over the FY 2022 CR level. Opioid use is not the only alarming trend in addiction and overdose, the misuse of stimulants, such as methamphetamine, is also increasing; and deaths attributed to using these combinations are likewise increasing. Taking note of these trends, FY 2021 appropriation language expanded allowable used of HEAL funds to include research related to stimulant misuse and addiction. Identifying how opioids and stimulants interact in combination to produce increased toxicity will enhance our ability to develop medications to prevent and treat comorbid opioid and stimulant use disorders and overdoses associated with this combination of drugs. In addition to continued emphasis on the research ongoing under the HEAL Initiative, the National Institute on Drugs and Addiction (NIDA)[11] has been funding targeted research to ensure we understand how best to respond to the specific challenges that COVID-19 itself and the impact of the pandemic overall pose to substance use, addiction, and overdose.

Long COVID: REsearching COVID to Enhance Recovery (RECOVER) Initiative
Some people recover quickly and completely from SARS-CoV-2 infection. However, others endure persistent symptoms for weeks to months, sometimes called PASC or Long-COVID, and still others experience their first symptoms after a silent initial infection. The incidence of Long COVID is currently unknown, but potentially large given the number of individuals across the age spectrum who have been or will be infected. In December 2020, recognizing the urgency of this public health challenge, Congress appropriated $1.15 billion in supplemental NIH funding, available over four years, to support research into the long-term effects of SARS-CoV-2

[9] emergency.cdc.gov/han/2020/han00438.asp
[10] pubmed.ncbi.nlm.nih.gov/33031013/
[11] The FY 2023 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.

infection.

In February 2021, NIH launched the RECOVER Initiative[12] to support research toward better understanding of Long COVID and effective ways to treat and even prevent it. At the heart of the initiative is a SARS-CoV-2 Recovery Cohort that includes children and adults, including pregnant women, from diverse racial and ethnic groups. This meta-cohort weaves together research efforts across the country, including population health studies that existed before the pandemic, to follow more than 20,000 individuals through in-person visits. A digital health platform will enable participation of millions more individuals through electronic health record data and mobile health technologies, such as smartphone apps and wearable devices, which will be used to gather real-world data in real time.

With these coordinated cohorts and the resulting data that will be generated from them, NIH hopes to answer critical questions about the population burden of Long COVID, its clinical spectrum, and its biological basis, including risk factors. This information, coupled with a patient-centric approach, will inform strategies to improve recovery from SARS-CoV-2 infection and to treat Long COVID among those suffering from it.

Developing A Universal Influenza Vaccine

The influenza virus remains a deadly and costly pathogen, placing a substantial health and economic burden on the United States and across the world each year. In the United States, the Centers for Disease Control and Prevention (CDC) estimates that the disease burden of influenza has resulted in between 9.2 million and 35.6 million illnesses, between 140,000 and 710,000 hospitalizations, and between 12,000 and 56,000 deaths annually since 2010, all of which results in an estimated $27 billion in health costs. Current influenza vaccination strategies rely on the development of an annual vaccine targeting the circulating strains that are anticipated to spread in the United States. NIH supports a research portfolio with the ultimate goal of developing a universal influenza vaccine to generate robust, long-lasting protection against multiple subtypes of influenza, eliminating the need to update the vaccine each year and protect against newly emerging strains with pandemic potential. NIH-funded researchers are making progress toward this goal by utilizing several novel approaches to develop vaccine candidates for clinical testing. Building upon the success of mRNA vaccines developed during the COVID-19 pandemic, NIH is working to expand this concept to the development of a universal influenza vaccine. Additionally, NIH-supported researchers are actively identifying and developing novel adjuvants for influenza vaccines to increase their immunogenicity and effectiveness. Continued investment in this research will enable the development of universal influenza vaccines to protect millions of people from infection. The FY 2023 budget request includes $260.0 million for universal influenza vaccine research, an increase of $40.0 million above the FY 2022 CR level.

The necessity for considering health disparities in research and medicine

The COVID-19 pandemic has brought into sharp focus the dramatic health disparities that exist across the American population, in number and severity of cases and in vaccination rates. These disparities highlight structural causes, some based on failures of the biomedical research

[12] www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-makes-first-infrastructure-awards-support-research-post-covid-conditions

community that the NIH is actively working to identify and address. NIH continues to address disparities in health outcomes and in the biomedical workforce, both through bold new initiatives such as UNITE and through sustained focus on health disparities led by the National Institute on Minority Health and Health Disparities (NIMHD).

In March 2021, the NIH launched an effort to end structural racism and racial inequities in biomedical research through a new initiative called UNITE, which has already begun to identify short-term and long-term actions.[13] The UNITE initiative's efforts are being informed by 5 committees with experts across all 27 NIH ICs who are passionate about racial diversity, equity, and inclusion. These five committees are:

- Understanding stakeholder experiences through listening and learning
- New research on health disparities/minority health/health inequity
- Improving the NIH culture and structure for equity, inclusion, and excellence
- Transparency, communication, and accountability with NIH's internal and external stakeholders
- Extramural research ecosystem and changing policy, culture, and structure to promote workforce diversity

UNITE aims to establish an equitable and civil culture within the biomedical research enterprise and reduce barriers to racial equity in the biomedical research workforce. To reach this goal, UNITE is facilitating research to identify opportunities, make recommendations, and develop and implement strategies to increase inclusivity and diversity in science. These efforts will bolster the NIH's effort to continue to strive for diversity within the scientific workforce and racial equity on the NIH campus and within the extramural community.

The work of the UNITE initiative builds upon and complements the advances in health disparities research spearheaded by NIMHD. NIMHD is leading the advancement of the science of minority health and health disparities in several ways, such as by redefining minority health and health disparities research; developing a research framework that underscores the key health determinants, levels of influence, and domains of influence researchers should consider in conducting research on minority health and health disparities; and developing methods and measurements for minority health and health disparities research. The "NIH Minority Health and Health Disparities Strategic Plan (2021-2025)"[14] was developed by NIMHD, in collaboration with other NIH ICs, and outlines the agency's research, research-sustaining activities, and outreach priorities and goals for minority health and health disparities. The FY 2023 President's Budget request includes an increase of $400.0 million above the FY 2022 CR level to enhance the health disparity research agenda at NIMHD and other ICs.

One particular area of health disparities of ongoing NIH focus is maternal mortality and morbidity. In response to rising maternal mortality (MM) in the United States, the initiative known as IMPROVE (Implementing a Maternal health and PREgnancy Outcomes Vision for Everyone) will support research on how to mitigate preventable MM, decrease severe maternal morbidity (SMM), and promote health equity in the United States. The initiative invests in

[13] www.nih.gov/ending-structural-racism
[14] www.nimhd.nih.gov/about/strategic-plan/

studies to promote an integrated understanding of biological, behavioral, sociocultural, and structural factors that contribute to maternal morbidity and mortality and engages communities in the development of solutions to address the needs of pregnant and postpartum individuals. The research projects will incorporate local community needs and perspectives to expand and complement existing research efforts by developing, implementing, and evaluating community-tailored interventions to address health disparities in SMM/MM, as well as investigate biological, behavioral, sociocultural, and structural risk factors and mechanisms of the leading causes of SMM/MM. Through this multidimensional strategy, IMPROVE aims to build an evidence-based approach to reducing SMM/MM and its associated health disparities. In FY 2020 and 2021, the NIH awarded over $20 million to support 58 projects via IMPROVE. One cross-cutting NIH IMPROVE funding opportunity was announced in FY 2021 to identify biological, behavioral, sociocultural, and structural factors that contribute to disparities in maternal health. The initiative also encourages researchers to investigate the potential effects of emerging infections, such as SARS-CoV-2. The FY 2023 President's Budget request for IMPROVE is $30.0 million. In addition, the request includes $3.0 million for National Institute for Child Health and Human Development (NICHD) to support research on mitigating the effects of COVID-19 on pregnancies, lactation, and postpartum health with a focus on individuals from racial and ethnic minority groups.

A diverse biomedical workforce is critical to address health disparities.[15] Scientific workforce diversity drives biomedical innovation, facilitates translation of advances to enhance health, and prepares scientists and healthcare professionals to better serve an increasingly diverse U.S. population. Therefore, it is a priority at the NIH to create a scientific workforce that reflects the diversity of our nation and the populations the agency serves. Collaborations across the NIH are allowing the creation of new opportunities for future scholars and current researchers to advance their careers in health disparities research and transition into competitive research investigators. In one example, within the new UNITE initiative, the E committee aims to evaluate NIH extramural policies and processes to identify and change practices and structures that perpetuate a lack of inclusivity and diversity. Meanwhile, the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program is one of many other efforts at NIH to increase biomedical workforce diversity. The FIRST program aims to establish a more inclusive and diverse biomedical research workforce through support of cluster hiring and institutional culture change efforts. The transformational impact of building and sustaining a culture of diversity and inclusive excellence will be beneficial to the institutions and the biomedical research community more broadly. The FY 2023 President's Budget includes an increase of $16.0 million above the FY 2022 CR level for the Chief Officer for Scientific Workforce Diversity (COSWD) to enhance NIH's effort to diversify the national scientific workforce and expand recruitment and retention.

Research topics that need additional focus

In addition to maternal mortality and morbidity, there are other research topics of new or renewed focus at NIH that intersect with health disparities or that have been brought into focus during the COVID-19 pandemic. In particular, NIH is directing increased attention towards mental health, the health effects of climate change, nutrition, and firearms.

[15] www.pnas.org/content/112/40/12240

Mental Health

Mental illnesses are the fifth leading cause of disability in the United States, accounting for 6.6 percent of all disability-adjusted life years in 2019.[16] The NIH supports research on many facets of mental health including research on rapid interventions to reduce severe suicide risk, funding adaptive interventions to optimize adolescent mental health treatments, and aggregating data to address mental health disparities research gaps. In response to the pandemic, the NIH launched a project to support research focused on the social, behavioral, and economic impacts of COVID-19, which supports research on the secondary effects of the pandemic, such as financial hardship, reduced access to health care, and school closures.[17] The FY 2023 President's Budget requests $2,210.8 million for the National Institute of Mental Health (NIMH), an increase of $107.1 million from the FY 2022 CR level. The increase for NIMH includes targeted increases of $25.0 million to expand research on the impact of the COVID-19 pandemic on mental health, $5.0 million to undertake studies of the impact of social media on mental health, and $5.0 million to inform mental health treatment approaches, service delivery, and system transformation in support of the Administration's mental health initiatives.

Climate Change

As the climate continues to change, the risks to human health will grow, exacerbating existing health threats and creating new public health challenges. Global climate change is already directly and indirectly affecting human health in the United States and around the world. Impacts occur through changes to climate systems such as temperature, air and water quality, and extreme weather events, as well as through changes to the geography and timing of exposures. Climate change contributes to or exacerbates a wide range of health impacts, including non-communicable disease, injury and trauma, and infectious diseases. Although climate change affects everyone, certain populations are especially vulnerable to various impacts due to social determinants of health, including life stage, sex, underlying health status, access to health care, education, and economic, racial, and ethnically driven disparities. In this way, the climate change and health agenda is inextricably linked to health equity. Climate change impacts are the concern of NIH as a whole and are often at the intersection of multiple ICs. For this reason, NIH is developing an 'all of NIH' approach to building a solutions-driven climate change and health strategic framework that will build on past research investments. The NIH strategic framework will seek to understand the health impacts and factors that contribute to individual and community susceptibility, strengthen capacity for needed research and the development of a transdisciplinary workforce, and promote community-engaged research, translation, and dissemination to maximize efforts and outcomes among the United States and global communities most urgently affected. The FY 2023 President's Budget request includes a $100.0 million increase above the FY 2022 CR level for research on the human health impacts of climate change.

Transforming Nutrition Science

To reflect the priority NIH places on innovative, multidisciplinary nutrition research, in FY 2021, the NIH Director moved the Office of Nutrition Research (ONR) to the NIH Office of the Director (OD). As part of ONR's role in planning, coordinating, and tracking progress toward achieving the objectives of the 2020-2030 Strategic Plan for NIH Nutrition Research, seven

[16] Institute of Health Metrics and Evaluation. ghdx.healthdata.org/gbd-results-tool accessed October 2021.
[17] covid19.nih.gov/news-and-stories/covid19-ripple-effects

topic-based, NIH-wide Implementation Working Groups have been created to develop specific initiatives, improve coordination, and broaden cross-cutting NIH subject matter expertise in nutrition research. ONR and these groups will lead the implementation of the Strategic Plan, completed by the Nutrition Research Task Force last year. The FY 2023 President's Budget request is $97.2 million, an increase of $96.0 million over the FY 2022 CR level, for the OD to support the objectives of the Strategic Plan.

Dedicated funding is critical to ensure that the Office of Nutrition Research can operate effectively as a cross-cutting NIH entity and to accomplish the goals of the plan. Part of the funding will enable ONR to support large, time-limited, goal-driven projects of cross-cutting NIH interest developed in collaboration with the ICs that already fund nutrition research.

One new collaborative project is the Reducing Nutrition Health Disparities through Food Insecurity and Neighborhood Food Environment Research. This research will use precision regional implementation science and pragmatic research approaches to test strategies ensuring food security and access to healthy food to prevent disparities in a variety of diet-related diseases and conditions, such as cardiovascular disease, obesity, diabetes, and cancer. Elucidating the role of these social conditions on diet and nutritional status could help address and prevent diet-related health disparities and promote health equity.

Nutrition science research will also complement the Artificial Intelligence (AI) for Chronic Disease initiative, given that most chronic diseases are diet-related. The complexity of human nutrition demands that cutting-edge data science and system science methods be employed to move this field into the 21st century. Some of the funds requested will support new training programs in AI for Precision Nutrition that will focus on integration of the domains of precision nutrition, AI including machine learning, systems biology, systems science, Big Data, and computational analytics. The goal is to build a future workforce that will be able to use growing data resources to tackle complex biomedical challenges in nutrition science that are beyond human intuition.

Firearms Research

Violence is a widespread public health problem that has profound impacts on lifelong health, opportunity, and well-being. Violence results in higher risk of developing physical and mental conditions and for experiencing societal challenges. When firearms are involved with violent events, the risk for injury and mortality and acute or chronic physical, mental, and behavioral health conditions increases. In 2019, there were 39,707 firearm-related deaths in the United States. Six out of every 10 deaths were firearm suicides, and more than 3 out of every 10 were firearm homicides.[18] NIH is committed to supporting scientific research to understand and prevent firearm violence injury and mortality through public health interventions. In 2021, the NIH funded a range of types of firearm violence prevention such as suicide, intimate partner violence, and youth violence. Projects are also diverse in their inclusion of populations ranging from youth to older adults, Alaska Native populations, men and women, and those who are firearm owners or not. The FY 2023 request for firearm research is $25.0 million, $12.5 million above the FY 2022 CR level.

[18] www.cdc.gov/violenceprevention/firearms/fastfact.html

Measuring Sex, Gender Identity, and Sexual Orientation
The NIH recognizes the significant health disparities that continue to exist within sexual and gender minority (SGM) populations and remains committed to ensuring that these populations are included and represented in research across the NIH. Since its establishment in 2015, the Sexual & Gender Minority Research Office (SGMRO) together with NIH as a whole have made significant progress in developing initiatives and increasing research activities to benefit SGM populations. Though much progress has been made, there is still much more work to do in ensuring equitable representation and inclusion of SGM populations in research. Building on the significant progress since the inception of SGMRO and an ongoing National Academies of Sciences Engineering and Medicine (NASEM) consensus study on Measuring Sex, Gender Identity, and Sexual Orientation,[19] $2.0 million will be provided within the Office of the Director to support the establishment of the Center for Sexual Orientation and Gender Identity (SOGI) Research. The goal of the Center will be to disseminate best practices in SOGI data collection to be distributed on a government-wide basis.

Lessons learned – new ways of conducting research, new research mechanisms, workplace flexibilities that may enhance the ability to conduct research

In addressing the COVID-19 pandemic, NIH established public-private partnerships to develop and test vaccines, diagnostics, and therapeutics in record time, all while extending flexibilities to NIH grantees and employees. The biomedical research ecosystem has endured and overcome challenges that were unimaginable just two years ago. NIH is taking these lessons about what and how research can be done into account as the agencies look towards the future.

Advanced Research Projects Agency for Health (ARPA-H)
ARPA-H will be a key component to drive transformational innovation in health research. Modeled after the Defense Advanced Research Projects Agency (DARPA), ARPA-H will recruit visionary term-limited program managers who can identify and fund traditional and non-traditional partners to take on critical challenges that are unlikely to move forward quickly without this catalytic assistance. ARPA-H will leverage novel public-private partnerships, use directive approaches that will provide quick funding decisions to support projects that are results-driven and time-limited, and identify emergent opportunities through advanced systematic horizon scans of academic and industry efforts. Potential areas of transformative research driven by ARPA-H include development and implementation of accurate, wearable, ambulatory blood pressure technology, preparation of mRNA vaccines against common forms of cancer, or accelerating development of efficient gene/drug delivery systems to target any organ, tissue, or cell type – a zip code for the human body. Opportunities or obstacles identified by the Cancer Moonshot may become candidates for the new approach to transformational change offered by ARPA-H. The President's Budget request for ARPA-H for FY 2023 is $5.0 billion. As ARPA-H will be in the phase of rapid launch and expansion, having the FY 2023 funding available over a three-year period will be critical.

ARPA-H projects should be bounded in time, typically a few years with longer periods allowed for efforts that are highly complex. ARPA-H should expect that a significant fraction of its

[19] www.nationalacademies.org/our-work/measuring-sex-gender-identity-and-sexual-orientation-for-the-national-institutes-of-health

efforts will fail; if not, the organization is being too risk-averse. The best approach is to fail early in the process, by addressing key risks upfront. To determine which risks should be taken and to evaluate proposed programs and projects, ARPA-H should adopt an approach similar to DARPA's "Heilmeier Catechism,[20]" a set of principles that assesses the challenge, approach, relevance, risk, duration, and metrics of success.

The ARPA-H director should have substantial authority to act. To keep the entity vibrant, the director will serve a single term of five years. For ARPA-H to accomplish its goals, it will need to be provided by Congress with certain authorities parallel to those provided to DARPA, including the authority to recruit, attract with competitive pay, and quickly hire for a set term extraordinary Program Managers. Unlike DARPA's focus on a single customer, ARPA-H will need to create breakthrough innovations that serve an entire ecosystem and all populations. ARPA-H should have a senior leader responsible for ensuring issues of equity are considered in all aspects of ARPA-H's work—from scientific program development to staff recruitment and hiring.

Within the Department of Health and Human Services, it will be important for ARPA-H to collaborate with other key agencies—CDC, FDA, the Centers for Medicare and Medicaid Services, the Biomedical Advanced Research and Development Authority/Office of the Assistant Secretary for Preparedness and Response (BARDA/ASPR), the Office of Minority Health, the Administration for Community Living, the Agency for Healthcare Research and Quality, and the Health Resources and Service Administration (HRSA)—to identify critical needs and opportunities and to partner on complex projects that interact, for example, with public health infrastructure or medical regulation. DARPA should also play a role in advising ARPA-H on its experiences in driving breakthrough innovation and collaborating on specific projects of shared interest. In addition, it would be valuable to engage science-based agencies and departments, such as the National Science Foundation, the National Institute of Standards and Technology, and the Department of Energy.

It will be critical for ARPA-H to engage with the broader biomedical community, including patients and their care-givers, researchers, industry, community groups, and others, to understand the full range of problems and the practical considerations that need to be addressed for all groups and populations.

Workplace flexibilities

NIH and the biomedical research community continue to meet the challenges of developing safe and effective therapeutic treatments and vaccines, accurate and reliable testing technologies, and behavioral and community prevention practices in response to the COVID-19 pandemic. The community must also grapple with the unprecedented impacts and massive disruption to the research enterprise that the pandemic has created. Many NIH-supported research projects across the Nation ground to a halt as universities and other research institutions suspended operations during the height of pandemic-related lockdowns. In some instances, this has resulted in the loss of critical biological resources that will have to be recreated. Similarly, the research workforce, particularly early-career scientists, faces significant challenges as the opportunity to generate and collect data has been disrupted.

[20] www.darpa.mil/work-with-us/heilmeier-catechism

The COVID-19 pandemic, along with extensive mitigation measures, has adversely affected progress in many biomedical research settings. Evidence from multiple sources, including a survey NIH issued to its extramural research workforce, indicates legitimate concerns about career trajectory for early-career scientists. Therefore, within existing constraints of available funding, NIH plans to offer extra support to early-career scientists whose career trajectories have been significantly affected by the pandemic.[21] NIH is providing an opportunity for recipients of NIH Fellowship and NIH Career Development awards who have been affected by COVID-19 to request either no-cost or funded extensions. For funded extensions, grantee requests will be considered by each IC on a case-by-case basis based on grantee justification that the training or career development activities have been significantly hindered over and above lost research productivity that most individuals experienced because of COVID-19 related shutdowns, as well as availability of funds.

Advances in dissemination and implementation research and strategies

The past year has highlighted the need for clear and consistent communication about both why science is important and how the scientific process works. NIH has been working in many ways to better communicate with the public through mechanisms such as the Vaccine Hesitancy Initiative and Ending the HIV Epidemic. It is also vital that scientists share and make broadly available the results from publicly funded biomedical research. Through a new policy to establish expectations for NIH-funded researchers around responsible data management and sharing, NIH is further catalyzing the scientific process to accelerate revolutionary discoveries and medical breakthroughs.

Vaccine Hesitancy Initiative
NIH launched the Vaccine Hesitancy Initiative in December 2020 to support research strategies and interventions to address vaccine hesitancy, uptake, and implementation among populations who experience health disparities in the United States.[22] Research is needed to understand and address misinformation, distrust, and hesitancy regarding vaccines (e.g., SARS-CoV-2, pneumococcal, influenza, hepatitis B, human papilloma virus (HPV), and herpes zoster) among adults in the United States and territories. The initiative targets populations at increased risk for morbidity and mortality due to long-standing systemic health and social inequities and chronic medical conditions. NIH solicited community-engaged research to evaluate intervention strategies to facilitate vaccination uptake in clinical and community contexts; and address the barriers to increasing reach, access, and uptake of vaccinations among health disparity populations at high risk and likely to experience vaccine hesitancy.

The Community Engagement Alliance (CEAL) Against COVID-19 Disparities works closely with the communities hit hardest by COVID-19.[23] The CEAL research teams focus on COVID-19 awareness and education research, especially among African Americans, Hispanics/Latinos, and American Indians —populations that account for over half of all reported cases in the United States. They also promote and facilitate the inclusion and participation of these groups in

[21] grants.nih.gov/grants/guide/notice-files/not-od-21-052.html
[22] grants.nih.gov/grants/guide/notice-files/NOT-MD-21-008.html
[23] www.nhlbi.nih.gov/news/2020/COVID-19-nih-funds-community-engagement-research-efforts-areas-hardest-hit

vaccine and therapeutic clinical trials to prevent and treat the disease. The FY 2023 President's Budget request includes an increase of $70.0 million above the FY 2022 CR level for CEAL and other COVID-related research initiatives in other ICs, including NIMH, to expand research on the pandemic impacts on mental health, and NICHD, to fund research on COVID effects on pediatric health. In addition, as mentioned above, $3.0 million for NICHD is requested to support research on mitigating the effects of COVID-19 on pregnancies, lactation, and postpartum health with a focus on individuals from racial and ethnic minority groups.

Ending the HIV Epidemic (EHE)

HIV disproportionately affects populations and geographic areas throughout the United States. In 2016 and 2017, 50 percent of newly diagnosed HIV infections in the United States occurred in 48 counties, some territories, as well as 7 states which have a significant and disproportionate occurrence of HIV in rural areas. The EHE initiative aims to reduce new HIV infections in the United States by 75 percent by 2025 and to end the HIV epidemic by 2030. As part of the initial EHE response, the NIH Centers for AIDS Research (CFARs) and the HIV/AIDS Research Centers (ARCs) built on existing relationships with local health authorities, community-based groups, and other HHS agencies involved in the EHE initiative, including the CDC and the HRSA.[24] With these partners, researchers have identified and evaluated strategies to diagnose new cases of HIV, help connect people living with HIV or at risk of HIV acquisition with medical care and HIV prevention services, and ensure they continue to receive care to treat or prevent HIV. These locally focused activities have used proven HIV treatment and prevention tools including antiretroviral therapy that suppresses HIV to undetectable levels, which benefits people living with HIV and prevents sexual transmission of the virus to others (Undetectable=Untransmittable); pre-exposure prophylaxis (PrEP), a single pill that can reduce the risk of acquiring HIV by more than 95 percent when taken daily; and emergency post-exposure prophylaxis (PEP), which can prevent HIV infection if begun within three days of exposure and taken for an additional 28 days. As the original halfway point of this initiative approaches, it is clear that an expanded, diversified response is required to reach communities and populations that continue to be disproportionately affected by HIV. The NIH includes 27 national institutes, centers and offices with expertise to reach these populations with renewed efforts; this multi-institute response is centrally coordinated within the office of the NIH Director. The President's Budget includes a $10.0 million increase above the FY 2022 CR level to expand implementation research activities conducted by CFARs and ARCs.

The next steps in NIH's EHE response will include multiple synergistic and coordinated efforts that draw on lessons learned from past and ongoing CFAR and ARC projects, the perceived gaps in research infrastructure and workforce needs in many EHE and high HIV-burden jurisdictions, and a recognition of the persistent racial inequities in health access to HIV prevention and treatment services. Moving forward, NIH is keen to support novel research and study designs that are flexible and nimble in responding and addressing shifts in the HIV epidemic as they develop; those that incorporate new, innovative, and readily deployable technology resources; and those that intentionally include demographically diverse populations. Information dissemination and implementation science research studies are equally critical and will be prominent focus areas for NIH moving forward. Further, NIH is committed to increasing research capacity and developing a sustainable and diverse HIV research workforce, not just in

[24] www.nih.gov/news-events/news-releases/nih-bolsters-funding-hiv-implementation-research-high-burden-us-areas

EHE jurisdictions but beyond, to ensure that 2025 EHE targets are met. To this end, the inclusion of minority serving institutions and diverse investigators will be pursued. Strategies demonstrated to be implementable at additional, larger scale research locations will be shared as best practices to inform efforts in high HIV-burden jurisdictions.

Final NIH Policy for Data Management and Sharing
The novel coronavirus pandemic has highlighted the importance of making research data broadly accessible. But even as the world struggles with this acute global crisis, it is important to note that we are at an extraordinary time in biomedical science, where new technologies, data science, and understanding of fundamental biology are converging to accelerate the pace of discovery and medical advancement. Released October 2020, the Final NIH Policy for Data Management and Sharing represents the agency's continued commitment to share and make broadly available the results of publicly funded biomedical research.[25] Responsible data management and sharing is good for science; it maximizes availability of data to the best and brightest minds, underlies reproducibility, honors the participation of human participants by ensuring their data is both protected and fully utilized, and provides an element of transparency to ensure public trust and accountability.

Mandatory Pandemic Preparedness Plan

The FY 2023 President's Budget includes $81.7 billion in mandatory funding, available over five years, across the Office of the Assistant Secretary for Preparedness and Response (ASPR), CDC, NIH, and FDA to support the Administration's plan to transform U.S. capabilities to prepare for and respond rapidly and effectively to future pandemics and other high-consequence biological threats. Within this total, the Budget requests $12.05 billion in mandatory funding for NIH to carry out the activities described below to advance the Administration's vision for pandemic preparedness.

Preclinical research and development of prototype vaccines and therapeutics against high profile viral families ($4.0 billion)

There are multiple virus families without an available vaccine, and many viruses within these families have the potential to cause significant human disease. Since it is not feasible to fully characterize the over 120 viruses known to cause human disease and develop medical countermeasures (MCMs), targeted selection of prototype viruses from each family offers a viable pathway to gain knowledge that may be applicable to a particular virus family. Funding will support the prototype pathogen approach of National Institute of Allergy and Infectious Diseases (NIAID) to accelerate the discovery, design and development of prototype vaccines and vaccine platforms, antiviral drugs, monoclonal antibodies (mAbs), and novel immuno-adjuvants to provide protection against prototype pathogens selected from a preliminary group of viral families of concern. Increasing fundamental knowledge and developing MCMs for the prototype virus(es) not only improves preparedness efforts for high-risk pathogens, but also provides the strategy to develop MCMs for other viruses within a viral family should an outbreak occur.

[25] www.federalregister.gov/documents/2020/10/30/2020-23674/final-nih-policy-for-data-management-and-sharing-and-supplemental-information

Through targeted basic and applied research on prototype pathogens from each viral family, a solid foundation of knowledge and candidate MCMs will enable a rapid response to the next emerging or remerging pathogen that creates a public health emergency.

This initiative will initially support foundational research to better understand and characterize prototype pathogens, with the primary goal of rapidly advancing candidate vaccines and mAbs into Phase 1 and Phase 2 clinical trials. In addition, comprehensive reagents leading to the development of antigen-specific and serological assays would also be developed as necessary tools for vaccine development. These areas of research are part of an integrated process for developing safe and effective MCMs. Foundational research includes understanding viral biology and structure, host immune responses, mechanisms of immune evasion, correlates of protection, disease pathogenesis, mechanisms of disease transmission including identification of disease vectors, and studies to develop assays and animal models.

This foundational research will be leveraged to develop vaccines and mAbs against the prototype pathogens. Antigens/immunogens will be evaluated for proof-of-concept using multiple vaccine and mAb rapid technology platforms. For lead prototype vaccines, translational activities will include evaluation of immunogenicity and efficacy in animal models to optimize dose and schedule, development of assays and reagents, identification of surrogate markers or correlates of protection, and investigational new drug (IND)-enabling safety and toxicology studies. For mAbs, translational activities will include generation of antibody clones, structure-function analyses, *in vitro* testing, efficacy testing in animal models to optimize dose and schedule, and evaluation in IND-enabling studies such as tissue cross-reactivity, pharmacokinetics, antibody half-life, and effector function analysis. This initiative will also include process development, manufacturing, and release and stability testing of the most promising MCM candidates to advance into Phase 1/2 clinical trials. In the case of an outbreak or event, strategies for developing vaccines and mAbs against prototype pathogens could then be rapidly applied to other viruses within the same viral family.

Expansion of laboratory capacity and pilot cGMP manufacturing for Phase 1/2 clinical studies ($2.35 billion)

The expansion of manufacturing infrastructure is critical to supporting the development of MCM candidates discovered through NIH's prototype vaccine, mAb, and therapeutic initiatives. The safe operation of biomedical research infrastructure is costly for many reasons including specialized ventilation, plumbing, and electrical systems that ensure the safety of research personnel and the general public. The initial aim is to invest a significant portion of the funding to address those infrastructure needs where a gap in research support exists, and that would most likely have the greatest benefit to the Federal government in preparing for and responding to future pandemics.

The ability to rapidly develop MCMs against the preliminary group of viral families of concern is dependent on the ability to manufacture, in compliance with FDA's Good Manufacturing Practice (GMP) regulations, pilot lots of prototype MCMs of consistent quality and stability. The ability to contract outside manufacturing for the development of pilot lots can be challenging, especially during a pandemic or public health emergency where the demand for services can

exceed supply. NIAID plans to double the pilot plant GMP manufacturing capacity of the Dale and Betty Bumpers Vaccine Research Center (VRC), which will significantly increase the MCM candidates to advance to early clinical testing (increasing from an average of 3-4 candidates per year to 6-8 candidates per year). The expansion process would be initiated during the first year, in parallel with increased process development and clinical testing capacities. Candidates would be advanced through the pipeline to early clinical testing in future fiscal years.

Development and clinical evaluation (through Phase 2) of vaccines and therapeutics ($2.0 billion)

Clinical evaluation is the final phase in the integrated process for developing safe and effective MCMs. Funding will support the conduct of Phase 1 and Phase 2 clinical trials in human subjects to evaluate the safety and immunogenicity of the most promising vaccine and mAb products, by leveraging the NIH's existing clinical trial networks, which have sites throughout the world.

In addition, new programs will be launched to discover and develop therapeutic MCMs through preclinical and early clinical stages, positioning them for efficacy testing. This research will include broad spectrum antivirals against circulating viruses, new modalities (*e.g.,* nanobodies/nanodrugs), and a program of drug discovery.

The National Heart, Lung, and Blood Institute (NHLBI) will support viral MCMs by developing an integrated host-tissue-directed therapeutic development and testing platform with two strategic components: a) development and testing of up to 10 host-tissue-directed countermeasures, including a range of interventions necessary to protect as well as treat certain injured critical host-organ/tissue systems (*e.g.,* cardiac, pulmonary, vascular) that determine both short-term and long-term morbidity and mortality; and b) mechanistic studies linked to the clinical trials and that provide critically important, evidence-based insights into the appropriate selection of MCMs to be tested in specific patient populations and at specific time points in viral disease progression.

Establish, expand, and/or improve large and flexible clinical trials networks and infrastructure that can be rapidly ramped up for urgent needs and to generate real-world evidence on the performance of vaccines, therapeutics, and diagnostics ($1.7 billion)

Funding will support the expansion of clinical trial infrastructure critical to responding to a pandemic. Being able to rapidly enroll participants in clinical trials from a diverse and inclusive cross section of communities is vital to that effort. Specific actions that will leverage, maintain, and expand NIH's network of domestic and international outpatient and inpatient clinical trial sites include: investing in tools to ensure site readiness and facilitate the conduct of clinical trials; building expertise and capacity in underserved communities by enhancing preparedness of clinical facilities, training and supporting clinical research staff, and conducting Phase 2 and Phase 3 clinical trials; improving IT infrastructure to integrate health systems and to integrate real-world data around use of therapeutics; and enhancing clinical laboratory infrastructure for variant surveillance and genomic sequencing capabilities. Funding will allow the hundreds of

clinical trial sites that NIAID and NHLBI have used during the COVID-19 pandemic to be maintained or stabilized as a warm base for future clinical trials.

Biosafety and biosecurity ($1.0 billion)

In the last decade, biosafety level (BSL)-3/4 laboratories have been essential to the development of MCMs in response to outbreaks caused by Ebola virus, Zika virus, and now SARS-CoV-2. The demands of the COVID-19 pandemic have stretched these labs to the limits of their capacities and response capabilities. Investments are needed to ensure that research and development for pandemic preparedness can be conducted safely and securely. Funding would be used to sustain the capabilities of BSL-3/4 laboratories with the appropriate subject matter expertise (i.e., emerging infectious diseases, specific pathogens) and/or capabilities needed for pandemic preparedness, and to construct, expand, upgrade and/or modernize aging infrastructure. This will include creating a BSL-3 and BSL-4 laboratory at the National Center for Advancing Translational Sciences (NCATS) for MCM screening and discovery, with a repository of approved and experimental clinical trial-stage MCMs for rapid response testing.

Develop innovations in early warning and affordable, accessible, and novel diagnostics, including pathogen-agnostic clinical and environmental surveillance technologies ($1.0 billion)

The RADx-Tech program for COVID-19 diagnostics development at the National Institute of Biomedical Imaging and Bioengineering (NIBIB) has provided over 1.7 billion COVID-19 tests to the U.S. as of January 2022. Critical gaps remain to be filled, requiring development of next-generation tests and technologies. Rapid antigen tests require serial use to give a reliable result and at-home molecular tests are costly. RADx-Tech will accelerate innovations in technology and manufacturing to develop affordable at-home tests with accuracy equal to lab-based polymerase chain reaction (PCR) tests. With the continued emergence of viral variants, new diagnostics must be designed that can rapidly pivot to new SARS-CoV-2 variants and new pathogens when needed. Further, RADx-Tech proposes to develop at-home tests that are easy to use for the aging population and those with disabilities, so that at-home testing is accessible to all. As COVID-19 becomes endemic, multiplex tests that can distinguish COVID-19, influenza, and other respiratory diseases will be invaluable for directing the right treatment to patients early in their infection.

There is also a continuing need to monitor and evaluate SARS-CoV-2 variants for potential impact on diagnostic test performance as well as optimize testing technologies for variant surveillance. RADx established an interagency Variant Task Force (VTF) in January 2021. To date, the VTF has brought together the extensive RADx public-private partnership with an interagency group from FDA, CDC, ASPR, and NIH. The VTF thoroughly characterized the impact of the omicron variant on performance of all marketed tests (both lab and clinical), and tests that did not detect omicron reliably were removed from the market. The VTF also developed a genotyping surveillance method that is lower cost than sequencing and gives more immediate information about the presence and spread of variants. The recent surge of omicron underscores the need for funding to maintain the VTF capability to detect and respond to future variants and pathogens.

Conclusion

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

NIH investments in research stimulate increased private investment. A $1.00 increase in public basic research stimulates an estimated additional $8.38 of industry R&D investment in a particular research area after 8 years.[26] In rural states, each $1.00 of NIH spending generated an average $1.80 of total economic impact. This economic activity then generates significant revenues for state and local governments, an average of $22 million per state in 2017 for applicable taxes and fees paid by businesses and employees.[27]

A healthier nation is a more productive and economically sound nation. Each permanent 1 percent reduction in cancer deaths alone has been approximated to have a value of nearly $500 billion to current and future generations of Americans. A full cure could be worth more than three times today's GDP.[28]

As the largest supporter of biomedical research in the world, with a history of catalyzing major breakthroughs over many decades, including the development of COVID-19 vaccines in record time, NIH looks forward in FY 2023 to continuing the tradition of bettering the human condition through rigorous and innovative science.

[26] sciencepolicy.colorado.edu/students/envs_5100/Toole2007.pdf
[27] www.unitedformedicalresearch.org/wp-content/uploads/2019/03/NIH-Research-Rural-States-Executive-Summary-FINAL-3.13.19.pdf
[28] ucema.edu.ar/u/je49/capital_humano/Murphy_Topel_JPE.pdf

OVERVIEW OF PERFORMANCE

The NIH mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Investments in basic biomedical and behavioral research make it possible to understand the causes of disease onset and progression, design preventive interventions, develop better diagnostics, and discover new treatments and cures. Realizing the benefits of fundamental biomedical discoveries depends on the translation of that knowledge into the development of new diagnostics, therapeutics, and preventive measures to improve health. Investments in translational research are leading to the identification of new targets and pathways for the development of new therapeutics.

The FY 2023 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. 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. They reflect NIH's ongoing efforts to address a variety of public health challenges and to further the U.S.'s biomedical research enterprise, including the need to identify effective prevention interventions for substance use disorders; support the development of diagnostic technologies and antiviral drugs to enhance pandemic preparedness; leverage health information technologies to improve minority health and reduce

health disparities; and diversify and foster the next generation of biomedical and behavioral scientists.

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 research capacity-building programs and 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 accounts for the majority 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 standing Working Groups.[29, 30] Ad-hoc working groups are established, as needed, to address emerging issues. The premise of the structure is that shared governance, which depends on the active participation of the IC Directors with the NIH Director, will foster the collaborative identification of corporate issues and a transparent decision-making process. With active participation by the IC Directors in NIH-wide governance, NIH can maximize its perspective and expertise in the development and oversight of policies common to NIH and its ICs. Through the governance process, corporate decisions are made; these may be long-term and strategic (e.g., facilities planning, budget strategy, 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.

[29] 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.
[30] The standing working groups are: Extramural Activities, Diversity, Facilities, Management and Budget, Scientific Data Council, Administrative Data Council, Data Science Policy Council, Clinical Center Governing Board, Board of Scientific Directors, and Research Services Working Group.

ALL-PURPOSE TABLE

National Institutes of Health
FY 2023 Congressional Justification

All Purpose Table
(Dollars in Thousands)

(Dollars in Thousands)[1,2]	FY 2021		FY 2022		FY 2023	
	Final[5]	**Supplemental Funding[6]**	**Continuing Resolution (CR)[7,8]**	**Supplemental Funding**	**President's Budget[7]**	**FY 2023 +/- FY 2022 CR**
Total, NIH Program Level	**$42,812,323**	**$1,250,000**	**$42,918,641**	**$0**	**$62,502,703**	**$19,584,062**
Less mandatory and funds allocated from different sources:						
PHS Program Evaluation	1,271,505		1,271,505		1,271,505	0
Mandatory Type 1 Diabetes Research[3]	150,000		141,450		141,450	0
Mandatory pandemic preparedness	0		0		12,050,000	12,050,000
Total, NIH Discretionary Budget Authority	**$41,390,818**	**$1,250,000**	**$41,505,686**	**$0**	**$49,039,748**	**$7,534,062**
Interior Budget Authority	81,500		81,500		83,035	1,535
Total, NIH Labor/HHS Budget Authority	**$41,309,318**	**$1,250,000**	**$41,424,186**	**$0**	**$48,956,713**	**$7,532,527**
Number of Competing RPGs	*11,258*		*9,806*		*11,878*	*2,072*
Total Number of RPGs	*41,613*		*41,145*		*43,129*	*1,984*
FTE[4]	*18,412*		*19,679*		*20,306*	*627*

[1] Numbers may not add due to rounding.
[2] Includes 21st Century Cures Act funding.
[3] Amounts in FY 2022 and FY 2023 reflect a reduction of $8.550 million for Budget Control Act sequestration.
[4] Includes 4 NIH FTEs funded by PHS trust funds in FY 2021 through FY 2023.
[5] Reduced by a transfer of $5.0 million from OD to the HHS Office of Inspector General and a Secretary's Transfer of $123.177 million.
[6] Reflects funding appropriated in P.L. 116-260.
[7] Reduced by a transfer of $5.0 million from OD to the HHS Office of Inspector General.
[8] Reflects the annualized amounts provided in the continuing resolution ending 3/11/2022.

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	**FY 2022 CR**[1]	**FY 2023 President's Budget**	**FY 2023 +/- FY 2022**
Research Project Grants	$24,185.206	$25,932.792	7.2%
Competing Average Cost (in thousands)	$571.465	$572.862	0.2%
Number of Competing Awards (whole number)	9,806	11,878	21.1%
Estimated Competing RPG Success Rate	16.9%	19.8%	17.2%
Research Centers	$2,774.182	$2,805.697	1.1%
Other Research	$2,880.055	$2,915.942	1.2%
Training	$983.585	$1,032.679	5.0%
Research & Development Contracts	$3,420.727	$3,568.852	4.3%
Intramural Research	$4,638.391	$4,763.453	2.7%
Research Management and Support	$2,145.807	$2,255.892	5.1%
Common Fund (non-add)	*$640.230*	*$658.539*	*2.9%*
Advanced Research Projects Agency for Health	$0.000	$5,000.000	NA
Pandemic Preparedness	$0.000	$12,050.000	NA
Buildings & Facilities Appropriation	$200.000	$300.000	50.0%
Other Mechanisms[2,3]	$1,690.686	$1,877.396	11.0%
Total, Program Level[4]	**$42,918.641**	**$62,502.703**	**45.6%**

[1] Reflects the annualized amounts provided in the continuing resolution ending 3/11/2022.

[2] 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.

[3] Amounts reflect directive transfer of $5.0 million to the HHS Office of Inspector General.

[4] Includes discretionary budget authority received from Labor/HHS appropriations bill and the Interior appropriations bill (Superfund). Also includes program evaluation financing and mandatory budget authority derived from the Type 1 Diabetes account and the Pandemic Preparedness Program.