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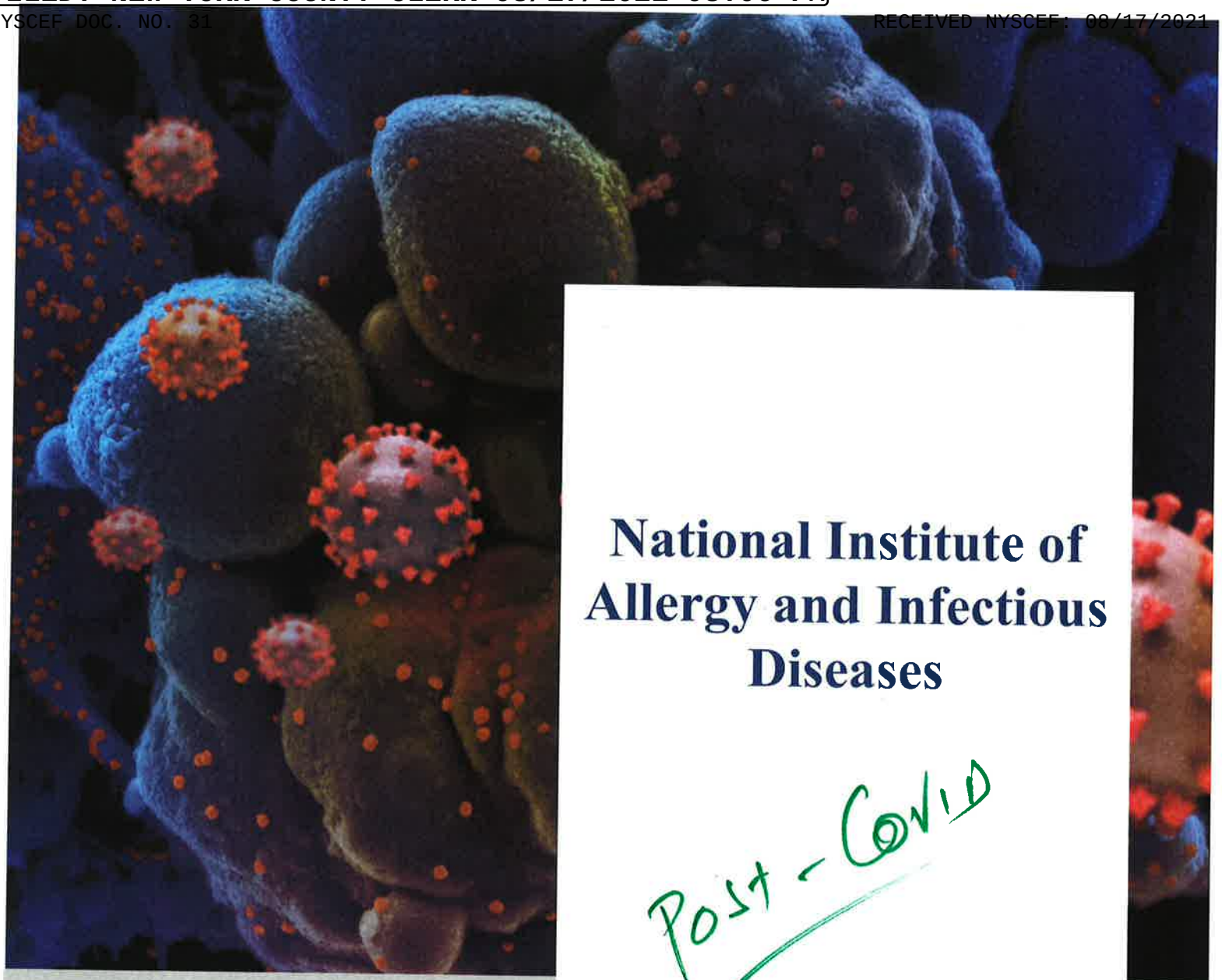


National Institute of Allergy and Infectious Diseases

Post-COVID

CONGRESSIONAL JUSTIFICATION
FY 2022

Department of Health and Human Services
National Institutes of Health

NIH National Institute of Allergy and Infectious Diseases

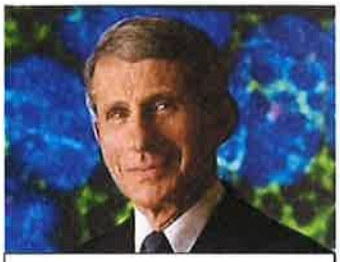
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases (NIAID)

FY 2022 Budget Table of Contents **Page No.**

Director's Overview


Anthony S. Fauci, M.D.

In 2020, the emergence of the novel coronavirus SARS-CoV-2 and the disease it causes, COVID-19, highlighted the importance of the dual mandate of the National Institute of Allergy and Infectious Diseases (NIAID). This mandate, to enable research on infectious, immunologic, and allergic diseases and respond to emerging public health threats, positioned NIAID at the forefront of research efforts to address the pandemic.

As the spread of SARS-CoV-2 and the increase in cases of COVID-19 continue globally, so too have NIAID's efforts to help control the outbreak. In leading the U.S. government's biomedical research response to the pandemic, the Institute is engaged in a multitude of activities focused on characterization of the virus and the disease it causes and the development of vaccines, therapeutics, and diagnostics.

Although SARS-CoV-2 emerged as a novel virus, prior NIAID-supported research on related viruses, including the viruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), provided a pivotal foundation for critical early studies on the SARS-CoV-2 virus. One study elucidated a key feature of the virus structure called the spike protein, which is expressed on the viral surface and initiates infection and may inform future treatment strategies. Research on the interaction between the virus and host target cells and in newly developed animal models has been complemented by observational studies to understand who is at higher risk of infection or disease and how the body responds to infection, particularly in vulnerable populations such as pregnant women, infants, the elderly, and people in high-risk occupations. Many of these studies require extensive collaborations across the federal government and with scientists in academia and pharmaceutical and biotechnology companies to address the breadth of clinical and public health issues posed by the current pandemic. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Heart, Lung, and Blood Institute (NHLBI), and NIAID are launching a multifaceted program to study the multi-system inflammatory syndrome (MIS-C) seen in some children following SARS-CoV-2 infection. These collaborations are critical for developing public health interventions to minimize the impact of the current pandemic and pave the way for preparedness efforts for future pandemics.

Basic information about SARS-CoV-2 and the immune response informs the development of rapid, accurate, and easy-to-administer diagnostics to mitigate the spread of COVID-19, such as those supported by the trans-NIH Rapid Acceleration of Diagnostics (RADx) initiative. In addition, NIAID is bringing together clinicians, scientists, and other federal agencies to improve and validate blood tests that detect antibodies to the virus. These tests are used in community-based and large-scale surveillance efforts—such as the RESPONSE study co-sponsored with NHLBI—to identify how many people have recovered from SARS-CoV-2 infection, providing data crucial for epidemiological models and public health decision-making.

Early on, the growing public health threat posed by SARS-CoV-2 underscored the need for rapid identification and testing of potential treatments for COVID-19. This includes identifying

existing licensed drugs that can be repurposed to treat COVID-19 and testing novel antiviral drugs, antibody-based therapies, and strategies to target an individual's immune response to the virus. In February 2020, NIAID launched the Adaptive COVID-19 Treatment Trial (ACTT), the first clinical trial in the United States to evaluate an experimental treatment for COVID-19. The adaptive trial design enables multiple therapies to be tested more efficiently and rapidly. The first iteration of ACTT demonstrated that remdesivir, an experimental broad-spectrum antiviral, accelerated the recovery of hospitalized patients with advanced COVID-19 disease. Subsequent iterations of ACTT are examining whether additional treatment strategies paired with remdesivir improve the body's response to infection. NIAID is coordinating the conduct of multiple clinical trials, including the trans-NIH Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership trials to examine monoclonal antibodies and other experimental therapeutics for diverse populations with varying severity of disease. Data from these studies will continue to inform the *NIH COVID-19 Treatment Guidelines* developed in collaboration with physicians, statisticians, public health experts, and community representatives.

NIAID is investigating multiple SARS-CoV-2 vaccine strategies, including technologies that have shown promise against coronaviruses that cause SARS and MERS. Based on encouraging results from early-stage clinical testing, NIAID and industry partner Moderna initiated Phase 3 clinical testing in late July of the mRNA-1273 vaccine candidate. The trial, which is being conducted at U.S. clinical research sites, enrolled approximately 30,000 adult volunteers who do not have COVID-19. NIAID also is supporting many other vaccine development studies with multiple partners in both industry and academia with the goal of creating a safe and effective vaccine. In response to this growing need for large-scale COVID-19 clinical trials, NIAID quickly leveraged its established research infrastructure and formed the NIH Coronavirus Prevention Network (CoVPN), a clinical trials network that aims to enroll thousands of volunteers in large-scale clinical trials testing a variety of investigational vaccines and treatments to protect people from COVID-19. The CoVPN was established by merging four existing NIAID-funded clinical trials networks that are focused on the prevention of HIV and other infectious diseases.

The emergence of COVID-19 as a global pandemic underscored the value of NIAID biomedical research preparedness efforts. NIAID-supported foundational research on related coronaviruses was pivotal in the rapid response to prevent and treat COVID-19. In addition, the experience in developing rapidly deployable vaccine platform technologies was critical to advancement of novel SARS-CoV-2 vaccine candidates at an unprecedented pace. However, one of the most effective preparedness strategies is detecting threats early and stopping them before they evolve into pandemics. As part of this effort, NIAID recently expanded its infrastructure to include the Centers for Research in Emerging Infectious Diseases, a global network dedicated to investigating how and where viruses and other pathogens emerge from wildlife and spillover to cause disease in people. Knowledge gained from research conducted by this network of investigators will support early warnings of emerging diseases wherever they occur and increase preparedness for future infectious disease outbreaks. Along with maintaining a flexible research infrastructure, NIAID will continue to advance its mission of protecting public health by preparing for and responding to emerging and re-emerging threats.

Overall Budget Policy:
As noted above, the importance of executing NIAID's dual mandate is underscored by its ongoing response to the COVID-19 pandemic. NIAID continues to support research and clinical trials to develop diagnostics, therapeutics and vaccines against COVID-19. Prior investments made through annual appropriations have positioned NIAID with the capability to rapidly respond to emerging and re-emerging disease threats such as COVID-19, Ebola, and Zika.

The FY 2022 President's Budget request seeks annual funding to continue support of NIAID's dual mandate to conduct and support basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases, while also supporting an infrastructure to respond to emerging and re-emerging public health and disease threats. The Institute dedicates its annual resources to support scientific opportunities that align with its mission and address domestic and global health problems and diseases.

The FY 2022 President's Budget request is $6,245.9 million, an increase of $178.9 million or 2.9 percent compared with the FY 2021 Enacted level. Within the President's Budget request, noncompeting grants will be funded at committed levels. The average cost of competing RPGs will be comparable to the FY 2021 level.

NIAID will continue to support basic and applied research to prevent, diagnose, and treat infectious and immune-mediated diseases and illnesses. Key research areas include emerging infectious diseases, agents with bioterrorism potential, HIV/AIDS, influenza, Ebola, tuberculosis, malaria, autoimmune disorders, drug-resistant microbes, asthma, and allergies. In FY 2022, NIAID will continue efforts to conduct foundational research on viruses and pathogens and to strengthen its infrastructure for investigating the origins of emerging infectious diseases and how they cause disease and illness. NIAID will also support opportunities for new researchers to receive R01 funding equivalent to those of established investigators who submit new R01 applications.

NIAID will continue support for trans-NIH initiatives, including a new cybersecurity effort, as well as other HHS-wide initiatives through the Research and Development contract mechanism. The Intramural Research Program will receive an increase to support critical long-range priorities with resources aligned to key research on infectious diseases such as HIV/AIDS, malaria, and influenza, as well as on combatting antibiotic-resistant bacteria (CARB).

National Institute of Allergy and Infectious Diseases

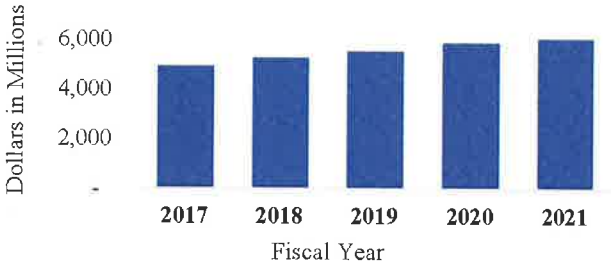
NIAID OVERVIEW

NIAID supports research to better **understand, treat, and prevent infectious, immunologic, and allergic diseases** while continuing in its unique dual mandate to respond rapidly to emerging and re-emerging diseases. For more than 65 years, NIAID research has led to new therapies, vaccines, diagnostics, and other technologies that have improved the health of millions of people in the United States and around the world.

NIAID DIRECTOR

Anthony S. Fauci, M.D.

NIAID APPROPRIATIONS HISTORY



FY 2022 President's Budget request is $6,245.9 million.

FACTS AND FIGURES*

1,945 Full-Time Equivalents

1,289 Funded Principal Investigators

*averages FY17-FY20

Research Highlights

NIAID is leading the U.S. government research response to COVID-19, including advancing basic research on SARS-CoV-2, diagnostics, and the development and testing of promising treatments and vaccines.

Researchers confirmed that reducing viral loads in people with HIV to undetectable levels with antiretroviral therapy (ART) can prevent the sexual transmission of the virus to others. Optimization and implementation of targeted treatment and prevention strategies in geographic "hot spots" could theoretically end the HIV epidemic in the United States.

The PALM (Pamoja Tulinde Maisha) trial in the Democratic Republic of the Congo revealed that two therapeutic agents improved survival in patients with Ebola virus disease.

NIAID researchers conducted the first-in-human clinical trial of a promising universal influenza vaccine.

Scientists identified a new approach to prevent the development of peanut—and possibly other—food allergies.

National Institute of Allergy and Infectious Diseases

Research Advances

LONG-ACTING PREVENTION OF HIV/AIDS

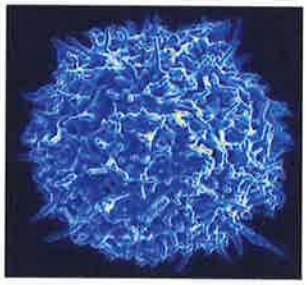
- Decades of NIAID-led research established effectiveness of pre-exposure prophylaxis (PrEP) to prevent HIV infection.
- NIAID is investing in research on long-acting forms of HIV prevention which are easy to access and use consistently for diverse populations.
- Several promising long-lasting prevention methods are being explored including:
  - A vaginal ring that releases the drug dapivirine over the course of 1 month.
  - Injectable drug cabotegravir, given once every 8 weeks, more effective than daily PrEP regimen
- Additional strategies being investigated: Implants, multi-purpose products that include contraception, broadly neutralizing antibodies, and others

HIV Pre-Exposure Prophylaxis (PrEP)

1 pill/day → **> 95%** effective in preventing HIV acquisition

Current HIV PrEP strategies are effective but require daily treatment regimen

CELL THERAPIES FOR IMMUNE-MEDIATED DISORDERS



Scanning electron micrograph of a human T cell from the immune system of a healthy donor. In multiple sclerosis, T cells are involved in the immune system's attack on the central nervous system.

- Cell therapy: Using stem cells or more specialized cells to treat disease
- Bone marrow transplants are standard lifesaving treatment for infants born with severe combined immunodeficiency, a rare genetic disorder
- Cell therapies could treat severe immune-mediated disorders
- Recent results show infusing hematopoietic (blood-forming) stem cells to reprogram a patient's immune system is an effective and durable treatment for people with severe relapsing-remitting multiple sclerosis (MS)
- Current large trial comparing this treatment to the best available MS therapies could not only provide a new treatment for this severe form of MS but also open doors for treating other autoimmune disorders, such as lupus.

PANDEMIC PREPAREDNESS

- Pandemic response relies on extensive NIAID biomedical research preparedness efforts
- Foundational research on coronaviruses pivotal to rapid response to prevent and treat COVID-19
- Recently established Centers for Research in Emerging Infectious Disease: a global network to investigate how and where viruses and other pathogens emerge from wildlife and spillover to cause disease in people, and enable early warnings of emerging diseases
- NIAID research and flexible infrastructure crucial to protect public health by preparing for and responding to emerging and re-emerging infectious diseases

Major Changes in the Fiscal Year 2022 President's Budget Request

Major changes by selected budget mechanism are briefly described below. The FY 2022 President's Budget is $6,245.9 million, an increase of $178.9 million or 2.9 percent compared with the FY 2021 Enacted level. Within this request level, NIAID will pursue its highest research priorities through strategic investments and careful stewardship of appropriated funds.

Research Project Grants (RPGs) (+$75.5 million; total $3,709.0 million):
NIAID will support a total of 5,654 Research Project Grant (RPG) awards in FY 2022. The increased funding will support research in NIAID's Biodefense and Emerging Infectious Diseases, Infectious and Immunologic Diseases, and HIV/AIDS program areas. The FY 2022 request reflects a resource shift from competing to noncompeting RPGs because of the FY 2021 re-competition of the HIV/AIDS Clinical Trials Networks (CTNs), which involve large-scale, multi-site clinical research activities. The HIV/AIDS CTNs continue as noncompeting grants in FY 2022. Funding for competing RPGs is expected to decrease by $191.6 million or 17.7 percent in FY 2022, while noncompeting RPG funding will increase by $263.3 million or 11.0 percent. Overall RPG funding will increase by 2.1 percent.

Research Centers (+$13.8 million; total $93.7 million):
The FY 2022 budget request provides an additional $10.0 million for the NIH Centers for AIDS Research (CFARs) to support the U.S. Department of Health and Human Services initiative, "Ending the HIV Epidemic in the U.S." (EHE). The initiative seeks to reduce new HIV transmissions by 75 percent over the next 5 years and by 90 percent within the next 10 years.

Other Research (-$36.5 million, total $94.4 million):
NIAID will reduce Other Research funding by 27.9 percent compared with the FY 2021 Enacted level. NIAID's FY 2021 resources included a one-time $40.0 million investment in Regional Biocontainment Laboratories (RBL), which was divided evenly among 12 RBLs to support efforts to prevent, prepare for, and respond to infectious disease outbreaks.

Research Training (+$4.4 million; total $69.7 million):
NIAID's FY 2022 budget request provides $4.4 million to support anticipated increases in training costs. The Ruth L. Kirschstein NRSA budget reflects a 2.0 percent stipend increase to cover cost of living expenses and additional resources for childcare allowances. NIH began providing childcare support to recipients of NRSA fellowships in FY 2021 and will introduce childcare allowances for NRSA-supported trainees in FY 2022.

Research and Development Contracts (+$85.8 million; total $1,072.8 million):
NIAID will continue to support trans-NIH initiatives, including a new cybersecurity effort, as well as other HHS-wide initiatives.

Intramural Research (+$24.7 million; total $807.5 million):
NIAID will increase funding to support critical long-range priorities with funds carefully aligned to key research on infectious diseases, such as HIV/AIDS, malaria, and influenza, as well as on CARB. Funding will also support the proposed FY 2022 pay raise for intramural research employees.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		FY 2022 +/- FY 2021 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	3,441	$2,556,855	3,675	$2,386,571	3,619	$2,649,684	-56	$263,112
Administrative Supplements	*(63)*	6,860	*(63)*	6,811	*(64)*	7,037	*(1)*	227
Competing:								
Renewal	188	134,439	183	184,607	203	149,148	20	-35,459
New	1,470	669,795	1,422	894,481	1,561	738,178	139	-156,303
Supplements	2	637	2	516	2	683	0	167
Subtotal, Competing	1,660	$804,871	1,607	$1,079,604	1,766	$888,010	159	-$191,594
Subtotal, RPGs	5,101	$3,368,586	5,282	$3,472,986	5,385	$3,544,730	103	$71,745
SBIR/STTR	278	160,491	273	160,536	269	164,301	-4	3,765
Research Project Grants	5,379	$3,529,077	5,555	$3,633,521	5,654	$3,709,031	99	$75,510
Research Centers:								
Specialized/Comprehensive	26	$70,652	25	$79,464	29	$93,218	4	$13,755
Clinical Research	0	931	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	765	0	500	0	512	0	12
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	26	$72,348	25	$79,964	29	$93,730	4	$13,767
Other Research:								
Research Careers	302	$51,134	305	$52,668	311	$54,247	6	$1,579
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	390	0	232	0	242	0	9
Other	87	34,440	107	77,980	83	39,911	-24	-38,070
Other Research	389	$85,965	412	$130,881	394	$94,399	-18	-$36,482
Total Research Grants	5,794	$3,687,390	5,992	$3,844,366	6,077	$3,897,160	85	$52,794
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	252	$11,748	254	$12,100	254	$12,522	0	$422
Institutional Awards	902	51,723	920	53,275	920	57,208	0	3,933
Total Research Training	1,154	$63,471	1,174	$65,375	1,174	$69,730	0	$4,355
Research & Develop. Contracts	198	$992,998	194	$987,024	211	$1,072,791	17	$85,767
(SBIR/STTR) (non-add)	*(24)*	*(19,691)*	*(26)*	*(20,590)*	*(30)*	*(22,141)*	*(4)*	*(1,551)*
Intramural Research	911	760,016	951	782,817	951	807,519	0	24,702
Res. Management & Support	1,058	372,320	1,100	387,489	1,100	398,726	0	11,237
SBIR Admin. (non-add)	*(0)*	*(907)*	*(0)*	*(2,370)*	*(0)*	*(2,370)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NIAID	1,969	$5,876,195	2,051	$6,067,071	2,051	$6,245,926	0	$178,855

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

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to allergy and infectious diseases, [$6,069,619,000]$6,245,926,000.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Summary of Changes

(Dollars in Thousands)

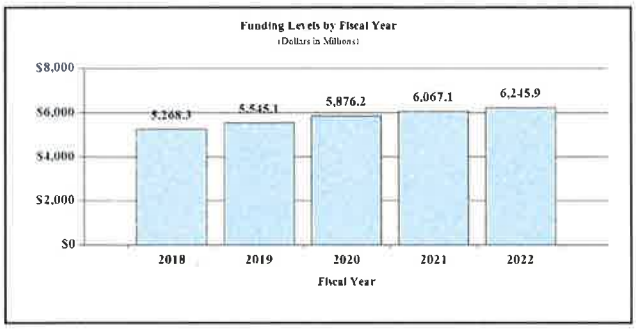
FY 2021 Enacted	$6,067,071
FY 2022 President's Budget	$6,245,926
Net change	$178,855

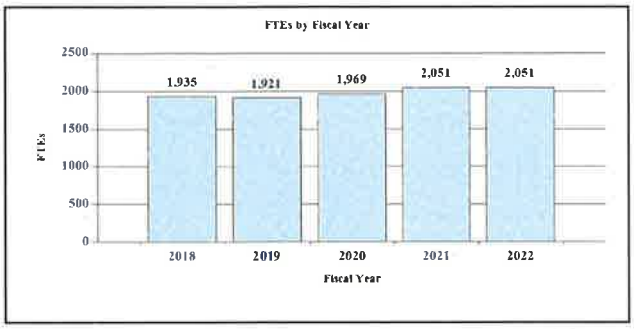
CHANGES	FY2021 Enacted		FY 2022 President's Budget		Built-In Change from FY 2021 Enacted	
	FTEs	Budget Authority	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:						
1. Intramural Research:						
a. Annualization of January 2021 pay increase & benefits		$199,937		$205,925		$545
b. January FY 2022 pay increase & benefits		199,937		205,925		5,441
c. Paid days adjustment		199,937		205,925		0
d. Differences attributable to change in FTE		199,937		205,925		0
e. Payment for centrally furnished services		108,484		113,908		5,424
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		474,397		487,686		10,341
Subtotal						$21,755
2. Research Management and Support:						
a. Annualization of January 2021 pay increase & benefits		$200,406		$206,502		$551
b. January FY 2022 pay increase & benefits		200,406		206,502		5,541
c. Paid days adjustment		200,406		206,502		0
d. Differences attributable to change in FTE		200,406		206,502		0
e. Payment for centrally furnished services		31,930		33,526		1,596
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		155,153		158,698		4,351
Subtotal						$12,050
Subtotal, Built-in						$33,804

CHANGES	FY2021 Enacted		FY 2022 President's Budget		Program Change from FY 2021 Enacted	
	No.	Amount	No.	Amount	No.	Amount
B. Program:						
1. Research Project Grants:						
a. Noncompeting	3,675	$2,393,382	3,619	$2,656,721	-56	$263,339
b. Competing	1,607	1,079,604	1,766	888,010	159	-191,594
c. SBIR/STTR	273	160,536	269	164,301	-4	3,765
Subtotal, RPGs	5,555	$3,633,521	5,654	$3,709,031	99	$75,510
2. Research Centers	25	$79,964	29	$93,730	4	$13,767
3 Other Research	412	130,881	394	94,399	-18	-36,482
4. Research Training	1,174	65,375	1,174	69,730	0	4,355
5. Research and development contracts	194	987,024	211	1,072,791	17	85,767
Subtotal, Extramural		$4,896,765		$5,039,681		$142,916
	FTEs		FTEs		FTEs	
6. Intramural Research	951	$782,817	951	$807,519	0	$2,946
7. Research Management and Support	1,100	387,489	1,100	398,724	0	-811
8. Construction		0		0		0
9. Buildings and Facilities		0		0		0
Subtotal, Program	2,051	$6,067,071	2,051	$6,245,926	0	$145,049
Total built-in and program changes						$178,855

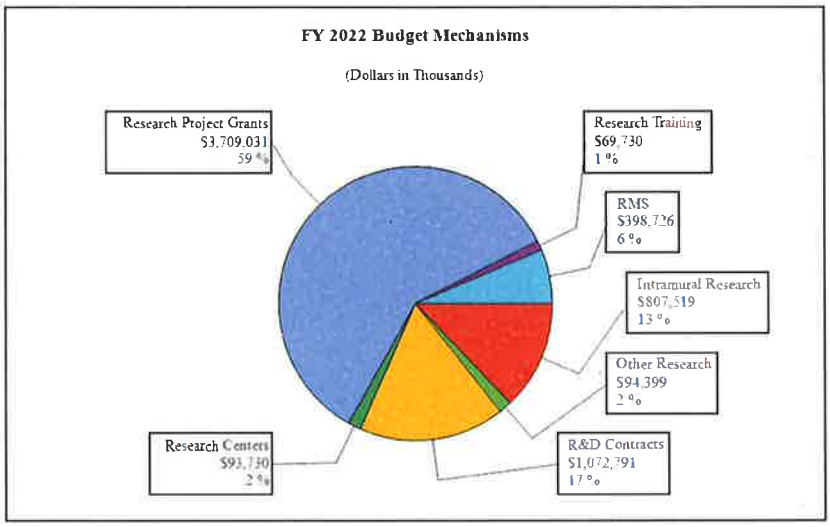
Fiscal Year 2022 Budget Graphs

History of Budget Authority and FTEs:

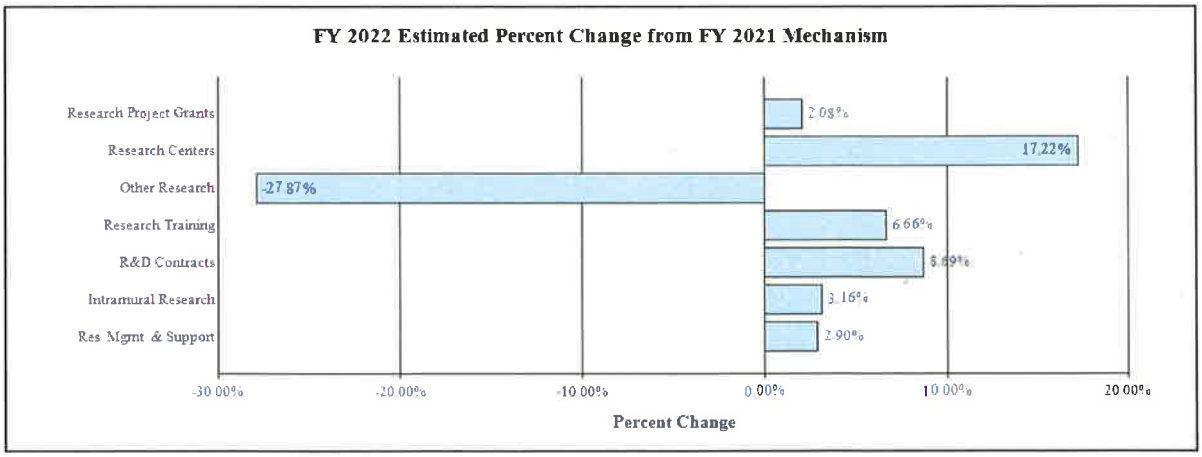


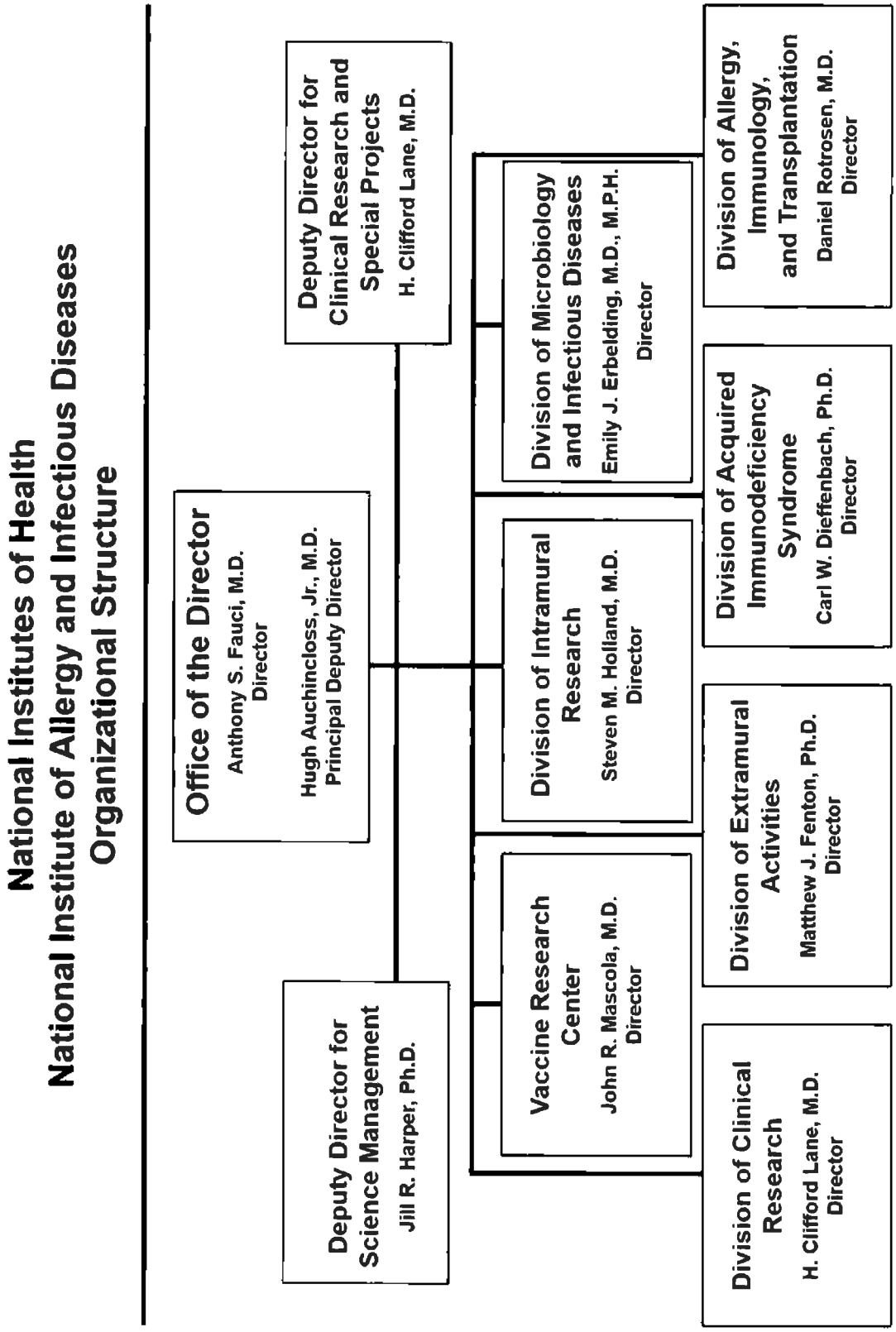


Distribution by Mechanism:



Change by Selected Mechanisms:




National Institutes of Health
National Institute of Allergy and Infectious Diseases
Organizational Structure
Office of the Director
Anthony S. Fauci, M.D.
Director
Hugh Auchincloss, Jr., M.D.
Principal Deputy Director
Deputy Director for Clinical Research and Special Projects
H. Clifford Lane, M.D.
Deputy Director for Science Management
Jill R. Harper, Ph.D.
Division of Microbiology and Infectious Diseases
Emily J. Erbelding, M.D., M.P.H.
Director
Division of Intramural Research
Steven M. Holland, M.D.
Director
Vaccine Research Center
John R. Mascola, M.D.
Director
Division of Clinical Research
H. Clifford Lane, M.D.
Director
Division of Extramural Activities
Matthew J. Fenton, Ph.D.
Director
Division of Acquired Immunodeficiency Syndrome
Carl W. Dieffenbach, Ph.D.
Director
Division of Allergy, Immunology, and Transplantation
Daniel Rotrosen, M.D.
Director

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Budget Authority by Activity[1]
(Dollars in Thousands)

	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		FY 2022 +/- FY 2021 Enacted	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
HIV/AIDS[2]		$1,429,914		$1,432,164		$1,431,821		-$344
Biodefense & Emerging Infectious Diseases[3]		1,924,809		2,029,781		2,114,771		84,990
Infectious & Immunological Diseases		1,389,136		1,434,820		1,493,090		58,270
Subtotal, Extramural		**$4,743,859**		**$4,896,765**		**$5,039,681**		**$142,916**
Intramural Research	**911**	**$760,016**	**951**	**$782,817**	**951**	**$807,519**	**0**	**$24,702**
Research Management & Support	**1,058**	**$372,320**	**1,100**	**$387,489**	**1,100**	**$398,726**	**0**	**$11,237**
TOTAL	**1,969**	**$5,876,195**	**2,051**	**$6,067,071**	**2,051**	**$6,245,926**	**0**	**$178,855**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

[2] Reflects NIAID extramural total for HIV/AIDS. NIAID-wide totals are (in thousands) $1,779,113 in FY 2020; $1,788,843 in FY 2021; and $1,798,843 in FY 2022.

[3] Reflects NIAID extramural total for Biodefense. NIAID-wide totals are (in thousands) $2,371,416 in FY 2020; $2,495,748 in FY 2021; and $2,594,251 in FY 2022.

Justification of Budget Request

National Institute of Allergy and Infectious Diseases

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

Budget Authority (BA):

	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 + / - FY 2021
BA	$5,876,195,000	$6,067,071,000	$6,245,926,000	+$178,855,000
FTE	1,969	2,051	2,051	0

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

Program Descriptions

HIV/AIDS

Decades of basic science and clinical research sponsored by NIAID have revolutionized the treatment of people with HIV/AIDS. With effective antiretroviral therapy (ART), a person with HIV now can expect a near-normal lifespan. Furthermore, individuals who receive ART and maintain an undetectable viral load (the amount of HIV in the blood) cannot sexually transmit the virus to others, a concept known as Undetectable = Untransmittable, or U=U. A single ART pill used daily as pre-exposure prophylaxis (PrEP) also can protect people who are at risk of acquiring HIV.

Implementing evidence-based treatment and prevention tools could theoretically end the HIV epidemic in the United States. The U.S. Department of Health and Human Services initiative, "Ending the HIV Epidemic in the U.S." (EHE), aims to reduce new HIV transmissions by 75 percent over the next 5 years and by 90 percent within the next 10 years. The strategy is focusing first on geographic and demographic "hot spots" where more than 50 percent of new HIV infections are concentrated. As part of the EHE initiative, NIAID is supporting research to optimize diagnosis, linkage to care, and treatment and prevention approaches for specific at-risk groups. This requires adapting implementation strategies to account for gender, cultural, and socioeconomic differences. In addition, NIAID provided supplemental and new funding to institutions participating in the trans-NIH Centers for AIDS Research and AIDS Research Centers programs. These awards will support pilot and exploratory studies aimed at enhancing knowledge needed for future implementation activities related to the EHE plan. In 2020, NIH added a program to include a focus on reducing HIV incidence by developing methods to improve PrEP uptake in cisgender women.

NIAID is investing in multiple approaches to prevent HIV, with the goal of delivering new options that are safe and effective, appeal to diverse populations, and are scalable worldwide to help end the global pandemic. Several long-lasting prevention methods are being explored, such as broadly neutralizing antibodies (bNAbs), vaginal rings containing an antiretroviral drug, and injectable therapeutics (see HIV Program Portrait), as well as implants and multi-purpose products that offer contraception along with HIV prevention. NIAID also is capitalizing on foundational investments and focusing on entirely new approaches to develop HIV vaccine candidates that elicit bNAbs, which usually develop in people years after HIV infection is established. These approaches use detailed knowledge of the structure of HIV proteins to create special immunogens—proteins that elicit an immune response. Identifying the fusion peptide—the section of the "spike" on the HIV surface that the virus uses to bind to and infect cells—and discovering that it is a target for bNAbs has led to the development of a vaccine candidate now being tested in humans for safety. Another vaccine in early testing uses a version of the HIV spike protein stabilized as a trimer—three proteins bound together—as it normally exists on the viral surface. A vaccine using a "mosaic" immunogen, created by stitching together multiple sections of the HIV genome, is being tested in two late-stage, multinational human clinical trials. Finally, NIAID scientists used a viral vector to deliver the gene for a bNAb. This technology can lead to the sustained production of that antibody for more than a year, as shown in a recent clinical trial. With further development, such a strategy could be applied to prevent, treat, and possibly induce a sustained remission in people with HIV.

LONG-ACTING APPROACHES FOR HIV PREVENTION

Currently, the only licensed PrEP regimen for people at risk of HIV infection is a daily pill regimen. Long-acting prevention methods may be more discreet, easier to use consistently, and easier to access and thus may increase the global uptake of PrEP. Two NIAID-supported clinical trials recently demonstrated that the drug cabotegravir, injected once every 8 weeks, was safe and more effective than a daily PrEP regimen in preventing HIV acquisition in men who have sex with men, transgender women, and cisgender women.

Large clinical trials are testing whether the bNAb VRC01, injected intravenously every 8 weeks, could provide long-lasting protection. Several other bNAbs developed by NIAID scientists also are being evaluated. A collaboration between NIAID and the nonprofit International AIDS Vaccine Initiative was created to systematically identify and assess bNAb combinations that can protect against a wide range of HIV strains.

Finally, clinical trials demonstrated that a vaginal ring that releases the drug dapivirine over the course of 1 month reduced women's risk of acquiring HIV. Further studies are examining the safety of the dapivirine ring during adolescence and pregnancy, when the risk of HIV acquisition is heightened. Long term, vaginal rings or implants could deliver drugs to prevent both pregnancy and HIV acquisition, thereby providing additional convenient choices for women.

Better treatment approaches are being tested that would facilitate long-term control of HIV. The long-acting antiretroviral drug cabotegravir has shown promise in clinical trials when given in conjunction with the antiretroviral rilpivirine. NIAID also is testing cabotegravir along with infusions of a newly designed bNAb given every 8 weeks. Treatment of HIV during pregnancy is particularly complicated, due to metabolic changes in the mother and the possibility that therapy will be toxic to the developing fetus. A large, NIAID-sponsored international trial recently demonstrated that ART regimens containing dolutegravir were more effective in

suppressing HIV and safer for the unborn infant than a different, commonly used regimen. This finding further supports the recently updated World Health Organization guidelines for HIV treatment during pregnancy. Further analyses of data from the trial will aid in understanding the factors affecting outcomes for both mother and infant.

Curing HIV is a major NIAID priority. This will require eradicating or otherwise controlling the HIV reservoir—pockets of virus that lie dormant in a small number of cells in the body and are activated when ART is interrupted. Studies in animal models recently identified two compounds that can activate these reservoirs. This activation could then enable the reservoir cells to be destroyed, an approach known as "kick and kill." NIAID also has partnered with NHLBI and the Bill & Melinda Gates Foundation to develop accessible gene-based cures for HIV as well as sickle cell disease.

Budget Policy:
The FY 2022 President's Budget request for the extramural component of the HIV/AIDS research is $1,431.8 million, which is $0.3 million below the FY 2021 Enacted level. NIAID will continue to support research from basic discovery through clinical trials on vaccine candidates as well as other treatment approaches that would facilitate long-term control of HIV. The FY 2022 request includes an increase of $10.0 million to prioritize the critical role of NIAID's Centers for AIDS Research program in the Department's efforts to end the HIV epidemic. As part of the EHE initiative, NIAID will continue research to optimize diagnosis, linkage to care, and treatment and prevention approaches for specific at-risk groups.

Biodefense and Emerging Infectious Diseases
The emergence and re-emergence of infectious diseases, accelerated by globalization and rapidly evolving microbes, continues to threaten the health of people worldwide. NIAID continues to conduct and support research to better understand viruses, bacteria, and other infectious agents that cause diseases of public health concern.

When Ebola virus disease (EVD) re-emerged in the Democratic Republic of Congo (DRC) in 2018, NIAID mobilized its flexible infrastructure and extensive experience establishing international collaborative research partnerships to advance several promising agents for preventing EVD, including the now-approved vaccine VSV-EBOV. As Ebola continues to re-emerge, with a new outbreak reported in June 2020 in the DRC, NIAID is continuing to advance the use, development, and testing of EVD vaccine candidates. In one study, NIAID scientists found that a single dose of a highly diluted VSV-EBOV vaccine remains fully protective against EVD in experimentally infected monkeys. These findings mean that VSV-EBOV may be effective at protecting against EVD at a much lower dose than anticipated, enabling more widespread availability of the vaccine. In addition, the lower dose could reduce the number of adverse reactions to vaccination, promoting its use. NIAID also is supporting the advancement of additional vaccine candidates against EVD, including vaccine platforms that provide protection against additional strains of filovirus as well as other hemorrhagic fevers endemic to overlapping regions in Africa.

The use of a single vaccine for a single virus has been a long-standing strategy to combat continually re-emerging threats, including seasonal influenza. However, each year, seasonal

influenza sickens millions and causes thousands of hospitalizations and flu-related deaths.[1] A NIAID high priority is the development of a safe and effective "universal" influenza vaccine that would provide long-lasting protection against multiple strains of the virus, including strains with the potential to cause a pandemic. NIAID is advancing several promising universal influenza vaccine candidates into clinical trials. One approach used by NIAID scientists is a combination of whole inactivated avian influenza viruses, which enables researchers to change virus components to optimize the mixture for a broadly protective immune response. Phase 1 studies of one such vaccine candidate will begin by late 2020 or early 2021. Another experimental vaccine candidate developed by NIAID researchers, called H1ssF_3928, displays part of the influenza hemagglutinin (HA) protein on the surface of a microscopic nanoparticle made of nonhuman ferritin. The HA protein consists of two regions, called the head and the stem. This vaccine utilizes the stem region, which does not vary much between influenza strains and is likely to generate immune responses that will be broader and long-lasting. Ferritin, a natural protein found in cells of all living species, is useful as a vaccine platform because it forms self-assembling nanoparticles that can display multiple influenza HA spikes on its surface, mimicking the natural organization of HA on the influenza virus. H1ssF_3928 displays HA molecules from group 1 influenza strains, one of two primary groups of influenza virus subtypes known to infect humans. Recently, H1ssF_3928 was tested in a Phase 1 clinical trial. In FY 2021, a counterpart to this nanoparticle vaccine for group 2 HA molecules will be similarly tested. Nanoparticle technology also is being leveraged by NIAID researchers in a separate universal influenza vaccine candidate. In this approach, HA molecules from multiple influenza strains are incorporated into nanoparticles. This vaccine strategy, called a "mosaic nanoparticle," may induce a broader immune response than current influenza vaccines. Researchers are planning a trial of this vaccine candidate in 2021.

In addition to nanoparticles, NIAID researchers recently tested a novel peptide-based candidate vaccine that is designed to prompt a different type of immune response to influenza viruses than most vaccines. The experimental vaccine, called FLU-v, targets several influenza proteins that tend to be similar across influenza strains. A Phase 2 trial of FLU-v showed that volunteers who received the investigational vaccine were less likely to develop mild to moderate influenza disease than volunteers who received a placebo. Advancement of these promising vaccine candidates underscores how NIAID-supported research in the areas of influenza virology, structural biology, protein engineering, immunology, and vaccinology have made possible the goal of advancing beyond strain-specific vaccines toward a universal influenza vaccine. In 2019, NIAID bolstered this effort by establishing the multidisciplinary Collaborative Influenza Vaccine Innovation Centers to advance the development of improved seasonal influenza vaccines and broadly protective universal influenza vaccine candidates. In the first year of the program, NIAID has advanced four novel influenza vaccine candidates into manufacturing for future clinical trials.

Another ongoing threat to public health is the growing presence of antibiotic-resistant infections. Each year, more than 35,000 people die in the United States alone from antibiotic-resistant infections.[2] Overuse and misuse of antibiotics drives the emergence and spread of resistance,

[1] CDC influenza information: www.cdc.gov/flu/about/burden/index.html
[2] CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.

resulting in bacterial infections that are difficult—and sometimes impossible—to treat. Under a seven-year grant renewal, the Antibacterial Resistance Leadership Group (ARLG), a global consortium that leads a comprehensive clinical research agenda, will place renewed emphasis on developing better countermeasures against antibiotic-resistant bacteria. ARLG also will support the development and evaluation of improved diagnostic tests to identify antibiotic-resistant microbes and studies to optimize use of existing antibiotics. A recent ARLG clinical study showed that a rapid antibiotic susceptibility testing method enabled markedly faster adjustments in antibiotic therapy for bloodstream infections with Gram-negative bacteria such as *E. coli* when compared to conventional testing. These tests could help physicians provide timely, effective therapy while supporting antibiotic stewardship to mitigate the development of antibiotic resistance.

The emergence of multidrug-resistant tuberculosis (MDR-TB), which is resistant to the two most effective anti-TB drugs, is a growing concern. However, recent progress in improved TB diagnostics, therapeutic regimens, and prevention approaches offer promise against this bacterial disease, which remains the leading infectious cause of death globally. A NIAID-supported macaque study using BCG, the only licensed TB vaccine, given intravenously (IV) instead of by the standard route of a needle placed just under the skin, resulted in a dramatic increase in vaccine efficacy. These data provide a model to better understand the immune markers and mechanisms of protection and support further investigation of IV BCG in clinical trials. Other TB vaccine candidates are advancing as well, and vaccines will be a powerful tool against drug-resistant strains. Current MDR-TB treatment regimens take 9 months or longer and may have substantial toxicity. Therefore, efforts to prevent latent TB infection from progressing to active MDR-TB are essential. To that end, a clinical trial is being conducted to compare the safety and efficacy of a new drug, delamanid, with that of the decades-old TB drug isoniazid for preventing active MDR-TB disease in people at high risk who are exposed to adult household members with MDR-TB. NIAID also is supporting a clinical trial to determine the optimal duration of an all-oral regimen for treating MDR-TB that may be better tolerated than current treatment strategies. TB also is the leading cause of death for people living with HIV. Although TB mainly affects those of reproductive age, pregnant women often are excluded from clinical trials, leaving gaps in our understanding of the impact of TB drugs on mothers and newborns. A recent NIAID-sponsored clinical study evaluated treatment with isoniazid in women with HIV during pregnancy or 12 weeks after delivery and compared outcomes for the mothers, fetuses, and newborns. Findings from this study helped inform strategies to safely prevent TB in women with HIV who are pregnant or have recently given birth.

Within the past decade, biennial spikes of a rare and sometimes serious condition called acute flaccid myelitis (AFM) have occurred in the United States. AFM is marked by sudden muscle weakness and paralysis, primarily in children. Many cases of AFM appear to be linked with non-polio enteroviruses, especially enterovirus D-68 (EV-D68), which usually causes only mild disease or asymptomatic infections. However, much about the disease remains unclear. In 2020, NIAID held a workshop to address the gaps in knowledge about AFM, including its possible cause(s) and the best avenues for developing therapies or preventive measures such as vaccines. A large, international study is ongoing to learn more about the incidence and distribution of this condition and to better understand how it develops and progresses in children. NIAID also is

supporting efforts to develop an effective EV-D68 vaccine candidate to combat the burden of this debilitating disease.

Tick-borne diseases remain a serious and growing public health problem in the United States. NIAID continues its commitment to research on Lyme disease and other tick-borne diseases through advancing research priorities outlined in the *NIH Strategic Plan for Tick-Borne Disease Research.* Among the key priorities is the improvement of diagnostics for tick-borne diseases, which are critical for optimal treatment. Results from a recent NIAID-supported study revealed that a new, rapid test for Lyme disease was more sensitive than current lab-based tests. These findings could translate into a faster, simpler, and more accurate point-of-care diagnostic for Lyme disease. NIAID also is advancing strategies to prevent the acquisition of tick-borne diseases. Along with human vaccines against tick-borne pathogens, this includes strategies that focus on reducing populations of ticks in the environment, as well as vector- and reservoir-targeted preventive approaches that can disrupt the transmission cycle of the pathogen. To advance these efforts, several new research projects focusing on the development of novel vaccine candidates and other innovative approaches for preventing Lyme and/or other tick-borne diseases were recently funded. For some tick-borne diseases, patients report long-term symptoms following treatment or in the absence of prompt treatment. Along with efforts to improve diagnosis and treatment, basic and clinical research projects will address key questions regarding why symptoms persist in some individuals, even after completion of treatment. NIAID will continue its efforts to bolster research and facilitate progress on this critical disease.

PREPARING FOR A PANDEMIC RESPONSE

Preparedness for emerging and re-emerging diseases requires an existing research infrastructure to enable a rapid and effective response. Critical to these efforts are networks that provide research and response capacity against emerging threats. In 2021, NIAID will establish the Centers of Excellence for Influenza Research and Response (CEIRR). The CEIRR program will focus on the study of influenza in humans and at the human-animal interface and will address knowledge gaps that can advance universal influenza vaccine research. The CEIRR also will provide international research infrastructure needed to address zoonotic influenza outbreaks in humans or a pandemic. In addition to known threats, the COVID-19 pandemic is a stark reminder of the ongoing threat of newly emerging pathogens.

When SARS-CoV-2 emerged as a public health threat, NIAID foundational research on "prototype" pathogens—the related coronaviruses causing SARS and MERS—provided critical background information to enable the rapid development of vaccines and therapies for this new coronavirus. In addition, existing research infrastructure, including the Centers for Translational Research, supported studies of the antiviral drug remdesivir, which was the first therapeutic demonstrated to improve outcomes for patients with severe COVID-19 disease.

For large-scale vaccine trials, NIAID built on existing HIV clinical research networks to establish the COVID Prevention Network. In FY 2020, in response to the growing number of threats spilling over from animal hosts, NIAID established the new Centers for Research in Emerging Infectious Diseases (CREID). This global network will advance our understanding of how and where viruses and other pathogens emerge from wildlife and cause disease in humans. The CREID network also will enable early warnings of emerging diseases, facilitating a rapid response and potentially curbing potential disease threats before they develop into widespread pandemics.

Budget Policy:
The FY 2022 President's Budget request for the extramural component of Biodefense and Emerging Infectious Diseases research supported by NIAID is $2,114.8 million, an increase of $85.0 million or 4.2 percent above the FY 2021 Enacted level. NIAID will continue to conduct and support research to better understand viruses, bacteria, and other infectious agents that cause diseases of public health concern. NIAID will promote basic and clinical research aimed at the development of vaccines, therapeutics and diagnostics for emerging and re-emerging infectious diseases including advancing a universal influenza vaccine and therapeutics against emerging infectious diseases and antibiotic resistant bacteria. FY 2022 resources will also support the development of medical countermeasures and new platform technologies against biodefense and emerging infectious disease pathogens.

NIAID will continue to prioritize the development of a safe and effective "universal" influenza vaccine that would provide long-lasting protection against multiple strains of the virus, including strains with the potential to cause a pandemic. NIAID is advancing several promising universal influenza vaccine candidates into clinical trials and is also advancing the use, development, and testing of EVD vaccine candidates to address the reemergence of Ebola. In addition, NIAID will continue research on Lyme disease and other tick-borne diseases through advancing research priorities as outlined in the *NIH Strategic Plan for Tick-Borne Disease Research.*

Infectious and Immunologic Diseases
NIAID conducts and supports basic and clinical research to better understand, diagnose, treat, and prevent infectious diseases and immune-mediated disorders—many of which have far-reaching global consequences—including malaria, neglected tropical diseases, hepatitis, TB, sexually transmitted infections (STIs), fungal diseases, autoimmune diseases, asthma, and allergic diseases.

Food allergy affects approximately 11 percent of adults and 8 percent of children in the United States, and many are allergic to more than one food.[3,4] Oral immunotherapy (OIT)—the repeated exposure to small, increasing amounts of an allergen in a controlled setting—can desensitize individuals, decreasing the likelihood of a severe allergic reaction. Based on promising results from a small study, NIAID recently launched the Omalizumab as Monotherapy and as Adjunct Therapy to Multi-Allergen Immunotherapy in Food Allergic Children and Adults, or OUtMATCH, study. This large clinical trial is testing whether the drug omalizumab injected every 2 or 4 weeks, either alone or with multi-allergen OIT, can increase a person's ability to tolerate multiple foods to which they are allergic. Sesame allergies, which often lead to severe reactions in children, are difficult to diagnose with standard allergy tests. Using data from antibody tests in children with food allergies combined with results of an oral food challenge, Scientists at NIAID developed a mathematical model to predict the probability that a child with food allergy also is allergic to sesame. Further studies will need to validate the model so that it

[3] Gupta RS, et al. *JAMA Netw Open* 2019 Jan 4;(2)1:e185630
[4] Gupta RS, et al. *Pediatrics* 2018 Dec;(142)6:e20181235.

can eventually be applied to clinical practice, which will allow doctors to better guide treatment for children with food allergies. Allergies are more likely to develop in people with atopic dermatitis, an immune disorder that causes red, itchy skin. However, some food allergy tests are less accurate in people with atopic dermatitis. To improve diagnosis, a new study aims to identify threshold levels of IgE (an allergic antibody) in blood samples from people with atopic dermatitis that would indicate an allergy to milk or peanut. Finally, two national surveys to assess awareness of and adherence to NIAID-led guidelines for peanut allergy prevention showed strong use of the guidelines by allergists and identified barriers to greater use by pediatricians.

STIs are a global public health challenge, with one million new cases of gonorrhea, syphilis, chlamydia, and trichomoniasis diagnosed each day worldwide.[5] Left untreated, STIs can result in serious health complications and often increase the risk of HIV transmission and acquisition. Additionally, increasing antimicrobial resistance will make STIs more difficult to treat as existing drugs become less effective. To facilitate the development of new and improved public health interventions, NIAID funded six new STI Cooperative Research Centers focusing on vaccine development for syphilis, gonorrhea, and chlamydia. NIAID also is translating results from basic research into clinical trials needed to move new interventions into clinical practice. For example, a large clinical trial was initiated to examine whether the antibiotic doxycycline taken soon after sexual contact without a condom is safe and effective against gonorrhea, chlamydia, and syphilis. Although doxycycline is approved by the U.S. Food and Drug Administration for other indications, this would expand its application to disease prevention in individuals at high risk of acquiring STIs. A recent Phase 2 clinical trial demonstrated that the investigational antibiotic zoliflodacin is effective against uncomplicated gonorrhea, which has progressively developed resistance to each of the current antibiotics used to treat it. Zoliflodacin is undergoing further testing against gonorrhea in a large, multicenter Phase 3 clinical trial sponsored by the Global Antibiotic Research and Development Partnership.

ADVANCING THERAPIES FOR MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is an autoimmune disease in which a person's own immune cells attack the central nervous system, causing neurological problems such as weakness, lack of coordination, vision loss, and problems with cognitive functioning or memory. Approved medicines for MS vary in effectiveness, safety, and cost. Advances in cell-based therapies have paved the way for their application in autoimmune diseases such as MS. In an approach called autologous hematopoietic stem cell transplantation (AHSCT), blood-forming stem cells are collected from the patient and the patient is then given high-dose chemotherapy to destroy their immune system. The person's own stem cells are then infused back to repopulate the individual's immune system, allowing a reset in which the new immune cells no longer attack the central nervous system. Previous studies supported by NIAID and others have suggested that AHSCT may be an effective and durable treatment for individuals with severe relapsing-remitting MS. A NIAID-supported clinical trial, called Best Available Therapy versus Autologous Hematopoietic Stem Cell Transplant for Multiple Sclerosis (BEAT-MS), will compare AHSCT to the best available biologics and other therapies for people with severe relapsing-remitting MS. Participants will be monitored for 6 years to assess disease severity and quality of life, and the newly developed immune system in participants undergoing AHSCT will be compared to the immune features of participants receiving best available (non–stem cell) therapies.

[5] Rawley J, et al. *Bull World Health Organ* 2019 Aug 1;(97)8:548-62.

Chronic infection with hepatitis B virus (HBV) can cause serious health problems, such as cirrhosis, liver failure, and liver cancer. Despite a highly effective preventive vaccine, approximately 257 million people worldwide are chronically infected.[6] NIAID recently led the development of a trans-NIH strategic plan to cure HBV [7]and reduce its sizable public health burden. The plan, released in fall 2019, includes strategic priorities to advance the understanding of HBV biology, develop needed tools and resources, and develop cure strategies.

Fungal infections such as coccidioidomycosis (Valley fever), histoplasmosis, and blastomycosis are particularly common in certain regions of the United States and can cause severe disease in healthy individuals. NIAID is addressing this growing health threat by encouraging fundamental research on fungal pathogens and the development and evaluation of therapies and diagnostics for these diseases. Currently, a Phase 1 clinical trial is enrolling healthy volunteers to evaluate the safety of various oral doses of the experimental anti-fungal drug VT-1598 and to understand how the drug is processed in the body.

Malaria, a mosquito-borne disease caused by *Plasmodium* parasites, causes symptoms including high fever, chills, and flu-like illness, and can be fatal. Approximately 2,000 cases of malaria are diagnosed each year in the United States. Worldwide in 2018, an estimated 228 million cases of malaria occurred and 405,000 people died of the disease, mostly children in Africa.[8] NIAID has a long-standing commitment to conduct and support research to reduce morbidity and mortality due to malaria and, ultimately, to eradicate the disease. Researchers at NIAID discovered and isolated a monoclonal antibody (mAb) against malaria, called CIS43, from a volunteer who received an investigational malaria vaccine. A Phase 1 clinical trial is assessing the safety and efficacy of a modified, more potent version of this mAb, CIS43LS, in healthy volunteers. Pregnant women are highly susceptible to malaria infection, which has substantial health risks for the woman, her fetus, and the newborn. However, no malaria vaccine trials have been conducted specifically in pregnant women or women of childbearing potential thus far. The PfSPZ malaria vaccine candidate has been shown to be safe in previous studies and will be tested in a Phase 2 clinical trial in women of childbearing potential during malaria transmission season in Mali. Women who become pregnant will be monitored for the duration of their pregnancy and babies and their mothers will be followed for one year after birth.

NIAID maintains a robust transplantation research program to improve the long-term success of organ, tissue, and cell transplantation. People with HIV have a growing prevalence of end-stage kidney disease and are nearly three times more likely to die while on kidney dialysis than people without HIV. Recently, a clinical trial supported by NIAID and the National Cancer Institute found that people with HIV who received a kidney transplant from a deceased donor with HIV had high overall survival and survival of the transplanted organ after 5 years. This study demonstrates that the pool of available kidneys for people with HIV can be expanded by including donors with HIV, making more kidneys available for all who are awaiting a transplant.

[6] WHO hepatitis B fact sheet: www.who.int/news-room/fact-sheets/detail/hepatitis-b
[7] https://www.niaid.nih.gov/sites/default/files/Trans-NIH-Hep-B-Strategic-Plan-2019.pdf
[8] CDC malaria information: www.cdc.gov/parasites/malaria/index.html

Budget Policy:
The FY 2022 President's Budget estimate for the extramural component of Infectious and Immunologic Diseases research is $1,493.1 million, an increase of $58.3 million or 4.1 percent above the FY 2021 Enacted level. NIAID will continue to advance long-range research priorities in infectious and immunologic diseases and to support basic and clinical research aimed at the development of countermeasures, such as therapeutics, vaccines, and diagnostics for emerging and re-emerging infectious diseases, including antibiotic resistant bacteria. The FY 2022 request will support NIAID's commitment and long-term interest in fundamental immunology and fund research on organ transplantation, malaria, neglected tropical diseases, hepatitis, TB, sexually transmitted infections (STIs), fungal diseases, autoimmune diseases, asthma, and allergic diseases.

Intramural Research Program (IRP)
The IRP remains at the forefront of efforts to translate basic science discoveries into new tools and strategies to improve human health and address urgent public health needs. The program has three components: 1) the Division of Intramural Research, comprising more than 125 principal investigators in Maryland and at the Rocky Mountain Laboratories in Montana who lead a wide range of basic, translational, and clinical research efforts; 2) the Vaccine Research Center, which applies fundamental advances to design and develop vaccines and biologic therapies against infectious diseases; and 3) the Division of Clinical Research, which plays an integral role in facilitating the efficient and effective performance of NIAID clinical research programs, both domestically and internationally, and in managing special projects as directed by the NIAID director.

The unique nature of the IRP, along with access to the NIH Clinical Center and longstanding U.S. and international partnerships, allows NIAID to execute high-risk and long-term studies and rapidly respond to global public health emergencies such as the recent Ebola outbreaks and the COVID-19 pandemic. Early during the COVID-19 response, studies conducted by NIAID researchers provided fundamental knowledge about SARS-CoV-2 structure, stability, and how the virus causes disease. Building on these studies, NIAID researchers, in collaboration with biotechnology company Moderna, based in Cambridge, Massachusetts, and researchers from the University of North Carolina at Chapel Hill, Vanderbilt University Medical Center in Nashville, and the University of Texas at Austin, conducted the preclinical research on a promising vaccine candidate, mRNA-1273. The mRNA-1273 vaccine is 94.1 percent efficacious in preventing symptomatic COVID-19 and was issued an Emergency Use Authorization (EUA) in December 2020. The vaccine has been administered to millions of people and is a critical tool for ending the COVID-19 pandemic. The rapid mobilization of this critical research infrastructure highlights the unique capacity and preparedness of the NIAID intramural research program to respond to public health emergencies.

In addition to responding to the COVID-19 pandemic, NIAID researchers continue to advance research with broad health impact, including studies targeted against diseases spread by vectors such as mosquitoes. Recently, NIAID scientists conducted a Phase 1 clinical trial of a promising candidate vaccine that targets components of mosquito saliva to prevent transmission of multiple mosquito-borne infections. In contrast to traditional vaccination strategies that are directed toward specific parasites, bacteria, or viruses, this strategy of targeting mosquito saliva could

provide broader protection against a variety of pathogens spread by mosquitoes. Intramural scientists also are leading research on the role of the microbiota—the community of microbes that colonize the human body in human health. Recent advances include new insights on the long-term effects of the microbiota in wound repair and an international study showing that a beneficial bacterium commonly found in probiotic digestive supplements helps eliminate *Staphylococcus aureus*, a type of bacteria that can cause serious antibiotic-resistant infections. Another study is investigating the possibility that immune responses to specific types of bacteria in the gut may predict which patients develop severe COVID-19 disease while others remain asymptomatic.

Basic research conducted by NIAID investigators provides the foundational knowledge that can be applied to the development of novel interventions to treat disease. In a highly collaborative study, NIAID scientists and their colleagues recently found that when the immune system first responds to infectious agents such as viruses or bacteria, a natural brake on the response prevents overactivation. This brake, a molecule called CD47, is turned on by certain pathogens including SARS-CoV-2 and is a potential target for broad-spectrum immunotherapies for infectious diseases. NIAID IRP researchers also collaborate with their NIH partners on a range of initiatives to advance groundbreaking discoveries, such as the trans-NIH Blood and Immune Deficiency–Cellular Therapy Program, launched in 2019, to systematically assess, treat, and monitor outcomes for patients with rare blood and immune disorders.

Budget Policy:
The FY 2022 President's Budget request for Intramural Research is $807.5 million, an increase of $24.7 million or 3.2 percent compared with the FY 2021 Enacted level. The FY 2022 Intramural Research plan supports NIAID's critical long-range research priorities with funding carefully aligned to support key research activities. These include continued support for all aspects of research on infectious diseases such as AIDS, malaria, and influenza, as well as research on causative agents, vectors, and the human host. In addition, NIAID is developing countermeasures against bioterrorism through basic research and its strong clinical research component, allowing vital lab discoveries to be rapidly translated into methods to prevent, diagnose, or treat disease.

Research Management and Support (RMS)
RMS activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. RMS activities include strategic planning, facilitation, and evaluation of Institute programs, as well as regulatory compliance, international coordination, and liaison activities with other federal agencies, Congress, and the public.

Budget Policy:
The FY 2022 President's Budget request for RMS is $398.7 million, an increase of $11.2 million or 2.9 percent compared with the FY 2021 Enacted level. The budget increase will support ongoing administrative efforts and cover the FY 2022 proposed pay increase.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2013	$4,495,307,000		$4,508,932,000	$4,490,711,484
Rescission				$8,981,423
Sequestration				($225,402,837)
2014	$4,578,813,000		$4,548,383,000	$4,358,841,000
Rescission				$0
2015	$4,423,357,000			$4,358,841,000
Rescission				$0
2016	$4,614,779,000	$4,512,918,000	$4,710,342,000	$4,629,928,000
Rescission				$0
2017[1]	$4,715,697,000	$4,738,883,000	$4,961,305,000	$4,906,638,000
Rescission				$0
2018	$3,782,670,000	$5,005,813,000	$5,127,866,000	$5,260,210,000
Rescission				$0
2019	$4,761,948,000	$5,368,029,000	$5,506,190,000	$5,523,324,000
Rescission				$0
2020	$4,754,379,000	$5,811,268,000	$5,937,816,000	$5,885,470,000
Rescission				$0
Supplemental				$1,542,000,000
2021	$5,885,470,000	$6,013,087,000	$6,142,540,000	$6,069,619,000
Rescission				$0
2022	$6,245,926,000			

[1] Budget Estimate to Congress includes mandatory financing.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2021 Amount Authorized	FY 2021 Enacted	2022 Amount Authorized	FY 2022 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$6,067,071,000	Indefinite	$6,245,926,000
National Institute of Allergy and Infectious Diseases	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$6,067,071,000		$6,245,926,000

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Amounts Available for Obligation[1]
(Dollars in Thousands)

Source of Funding	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
Appropriation	$5,885,470	$6,069,619	$6,245,926
Secretary's Transfer	0	0	0
Subtotal, adjusted appropriation	$5,885,470	$6,069,619	$6,245,926
OAR HIV/AIDS Transfers	-9,275	-2,548	0
Subtotal, adjusted budget authority	$5,876,195	$6,067,071	$6,245,926
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$5,876,195	$6,067,071	$6,245,926
Unobligated balance lapsing	-21	0	0
Total obligations	$5,876,174	$6,067,071	$6,245,926

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:
FY 2020 - $42,877 FY 2021 - $44,592 FY 2022 - $45,885

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Budget Authority by Object Class[1]

(Dollars in Thousands)

		FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021 Enacted
Total compensable workyears:				
	Full-time equivalent	2,051	2,051	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$200	$205	$5
	Average GM/GS grade	12.6	12.6	0.0
	Average GM/GS salary	$121	$124	$3
	Average salary, Commissioned Corps (42 U.S.C. 207)	$104	$107	$2
	Average salary of **ungraded positions**	$162	$165	$4
	OBJECT CLASSES	**FY 2021 Enacted**	**FY 2022 President's Budget**	**FY 2022 +/- FY 2021**
	Personnel Compensation			
11.1	Full-Time Permanent	180,599	184,708	4,109
11.3	Other Than Full-Time Permanent	77,930	79,703	1,773
11.5	Other Personnel Compensation	11,024	11,274	251
11.7	Military Personnel	4,488	4,612	125
11.8	**Special** Personnel **Services Payments**	25,820	26,408	587
11.9	**Subtotal Personnel Compensation**	**$299,860**	**$306,705**	**$6,844**
12.1	Civilian Personnel Benefits	96,714	101,849	5,136
12.2	Military Personnel Benefits	3,769	3,874	105
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$400,343**	**$412,427**	**$12,084**
21.0	Travel & Transportation of Persons	4,483	4,565	82
22.0	Transportation of Things	1,749	1,783	34
23.1	Rental Payments to GSA	6	6	0
23.2	Rental Payments to Others	68	69	1
23.3	Communications, Utilities & Misc. Charges	2,284	2,301	17
24.0	Printing & Reproduction	0	0	0
25.1	Consulting Services	203,536	212,389	8,853
25.2	Other Services	168,795	176,058	7,263
25.3	Purchase of goods and services from government accounts	617,358	648,297	30,939
25.4	Operation & Maintenance of Facilities	16,671	16,896	225
25.5	R&D Contracts	683,336	748,378	65,041
25.6	Medical Care	6,016	6,238	223
25.7	Operation & Maintenance of Equipment	28,999	29,609	610
25.8	Subsistence & **Support of** Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$1,724,711**	**$1,837,865**	**$113,153**
26.0	Supplies & Materials	49,991	51,309	1,318
31.0	Equipment	41,467	42,492	1,024
32.0	Land and Structures	959	976	17
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	3,841,001	3,892,125	51,124
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	8	8	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$5,666,728**	**$5,833,499**	**$166,771**
	Total Budget Authority by Object Class	**$6,067,071**	**$6,245,926**	**$178,855**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

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Salaries and Expenses

(Dollars in Thousands)

OBJECT CLASSES	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Personnel Compensation			
Full-Time Permanent (11.1)	$180,599	$184,708	$4,109
Other Than Full-Time Permanent (11.3)	77,930	79,703	1,773
Other Personnel Compensation (11.5)	11,024	11,274	251
Military Personnel (11.7)	4,488	4,612	125
Special Personnel Services Payments (11.8)	25,820	26,408	587
Subtotal Personnel Compensation (11.9)	**$299,860**	**$306,705**	**$6,844**
Civilian Personnel Benefits (12.1)	$96,714	$101,849	$5,136
Military Personnel Benefits (12.2)	3,769	3,874	105
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$400,343**	**$412,427**	**$12,084**
Travel & Transportation of Persons (21.0)	$4,483	$4,565	$82
Transportation of Things (22.0)	1,749	1,783	34
Rental Payments to Others (23.2)	68	69	1
Communications, Utilities & Misc. Charges (23.3)	2,284	2,301	17
Printing & Reproduction (24.0)	0	0	0
Other Contractual Services:			
Consultant Services (25.1)	203,536	212,389	8,853
Other Services (25.2)	168,795	176,058	7,263
Purchases from government accounts (25.3)	466,544	492,149	25,604
Operation & Maintenance of Facilities (25.4)	16,671	16,896	225
Operation & Maintenance of Equipment (25.7)	28,999	29,609	610
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$884,545**	**$927,100**	**$42,555**
Supplies & Materials (26.0)	$49,991	$51,309	$1,318
Subtotal Non-Pay Costs	**$943,121**	**$987,128**	**$44,007**
Total Administrative Costs	**$1,343,464**	**$1,399,555**	**$56,091**

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National Institute of Allergy and Infectious Diseases

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2020 Final			FY 2021 Enacted			FY 2022 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Acquired Immunodeficiency									
Direct:	151	8	159	155	7	162	155	7	162
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	151	8	159	155	7	162	155	7	162
Division of Allergy, Immunology, and Transplantation									
Direct:	99	-	99	103	-	103	103	-	103
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	99	-	99	103	-	103	103	-	103
Division of Clinical Research									
Direct:	91	9	100	90	8	98	90	8	98
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	91	9	100	90	8	98	90	8	98
Division of Extramural Activities									
Direct:	211	-	211	233	-	233	233	-	233
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	211	-	211	233	-	233	233	-	233
Division of Intramural Research									
Direct:	691	13	704	725	11	736	725	11	736
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	691	13	704	725	11	736	725	11	736
Division of Microbiology and Infectious Diseases									
Direct:	176	8	184	181	7	188	181	7	188
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	176	8	184	181	7	188	181	7	188
Office of the Director									
Direct:	390	2	392	412	2	414	412	2	414
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	390	2	392	412	2	414	412	2	414
Vaccine Research Center									
Direct:	119	1	120	116	1	117	116	1	117
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	119	1	120	116	1	117	116	1	117
Total	1,928	41	1,969	2,015	36	2,051	2,015	36	2,051
Includes FTEs whose **payroll obligations** are **supported by** the NIH Common **Fund.**									
FTEs supported by **funds from Cooperative Research and Development Agreements.**	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2018	12.6
2019	12.7
2020	12.6
2021	12.6
2022	12.6

NATIONAL INSTITUTES OF HEALTH
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Detail of Positions[1]

GRADE	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	394,600	400,618	409,732
General Schedule			
GM/GS-15	197	181	181
GM/GS-14	427	434	434
GM/GS-13	388	387	387
GS-12	229	243	243
GS-11	114	121	121
GS-10	1	1	1
GS-9	67	71	71
GS-8	26	28	28
GS-7	53	56	56
GS-6	5	5	5
GS-5	8	8	8
GS-4	8	8	8
GS-3	8	8	8
GS-2	0	0	0
GS-1	1	1	1
Subtotal	1,532	1,552	1,552
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	12	11	11
Senior Grade	12	11	11
Full Grade	9	9	9
Senior Assistant Grade	4	4	4
Assistant Grade	0	0	0
Subtotal	37	35	35
Ungraded	467	467	467
Total permanent positions	1,556	1,612	1,612
Total positions, end of year	2,038	2,056	2,056
Total full-time equivalent (FTE) employment, end of year	1,969	2,051	2,051
Average ES salary	197,300	200,309	204,866
Average GM/GS grade	12.6	12.6	12.6
Average GM/GS salary	119,355	121,175	123,932

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.