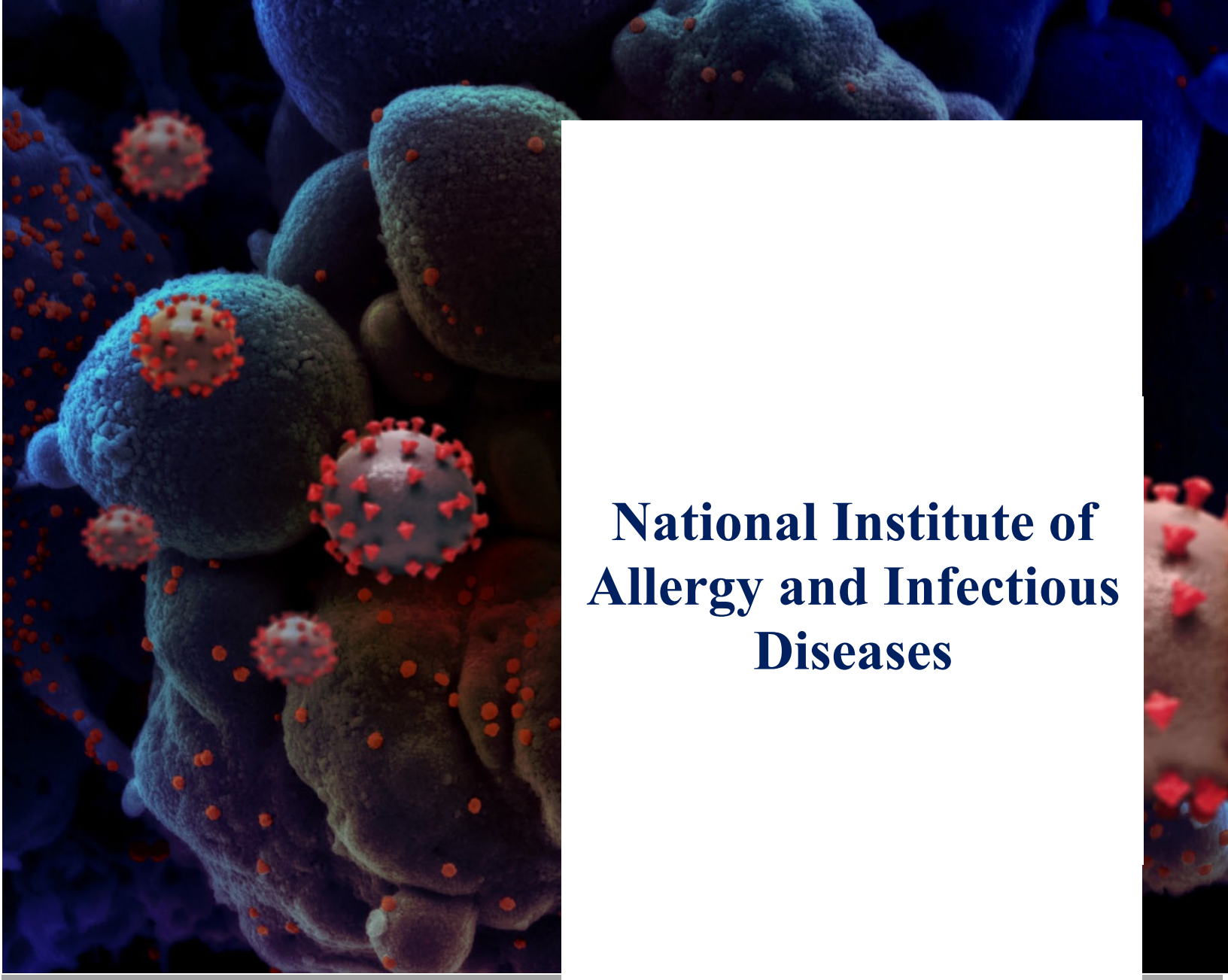

National Institute of Allergy and Infectious Diseases

CONGRESSIONAL JUSTIFICATION
FY 2023

Department of Health and Human Services
National Institutes of Health

NIH National Institute of Allergy and Infectious Diseases

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases (NIAID)

FY 2023 Budget Table of Contents

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Director's Overview

Anthony S. Fauci, M.D.

The National Institute of Allergy and Infectious Diseases (NIAID) has been at the forefront of research to address the COVID-19 pandemic while continuing to lead research on other diseases. NIAID is actively preparing for the emergence of new public health threats, including variants of SARS-CoV-2, the virus that causes COVID-19. These efforts reflect the dual mandate of NIAID, to enable research on infectious, immunologic, and allergic disease and respond to emerging public health threats with the overall goal of enhancing human health.

NIAID responded rapidly to the COVID-19 pandemic by mobilizing existing research programs, especially research on related coronaviruses, including those that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Coronaviruses have a spike protein on their surface that plays an essential role in infection. NIAID scientists designed a stabilized spike antigen based on their previous research on coronavirus spike structures. NIAID and the biotechnology company Moderna then developed a messenger RNA (mRNA) vaccine, which directs the body's cells to express the spike in its prefusion conformation to elicit an immune response. The Pfizer-BioNTech, Janssen, Novavax, and Sanofi vaccines are also based on the stabilized version of the spike protein.

Building on successes in the fight against COVID-19, NIAID is expanding on its already robust basic research portfolio to plan for emerging infectious disease threats. To mitigate risks associated with these yet unknown pathogens, NIAID is prioritizing preparedness research on prototype-pathogens, representative pathogens from viral families known to infect humans. Prototype pathogen research can be used to inform the development of medical countermeasures (MCMs), such as therapeutics, vaccines, and monoclonal antibodies (mAbs), for related viruses. In addition, NIAID continues to characterize and conduct preclinical testing of high priority pathogens most likely to threaten human health and advance platform technologies that also can be leveraged to develop MCMs. To further pandemic preparedness, NIAID established a global network of research centers to study how and when viruses and other pathogens emerge from wildlife and spillover into humans. The Centers for Research in Emerging Infectious Diseases (CREID) will enable early warnings of emerging diseases, facilitating a rapid response and potentially curbing potential disease threats before they develop into widespread pandemics. Additionally, NIAID continues the Pandemic Response Repository through Microbial and Immune Surveillance and Epidemiology (PREMISE) program that pairs virologic and immunologic surveillance of viruses and facilitate the development of diagnostic tests and MCMs in anticipation of potential pandemic threats.

Despite the challenges posed by COVID-19, NIAID's work to address the ongoing HIV epidemic has not wavered. Achieving a durable end to the HIV pandemic will require research on the optimal implementation of diagnosis, treatment, and prevention methods, as well as continued development of new and improved prevention and treatment tools suited to those

populations most affected by HIV. In 2020, NIH awarded approximately $10 million to advance the goals of *Ending the HIV Epidemic: A Plan for America*, which aims to reduce new HIV diagnoses in the United States by at least 90 percent by 2030. NIAID expanded the existing collaborative, multidisciplinary NIH-wide Centers for AIDS Research (CFARs) and AIDS Research Centers (ARCs) programs to stimulate new and improved diagnostics, prevention, and treatment options, particularly for populations in areas highly impacted by HIV. Stark disparities in HIV outcomes exist not only regionally, but also between certain age, racial, and ethnic groups, as well as among sexual and gender identities. Accordingly, NIAID is continuing efforts to include diverse populations at all stages of clinical research to develop culturally appropriate, tailored interventions that may help communities respond to the unique needs of people in—or at the intersections of—these groups.

The emergence of SARS-CoV-2 variants underscores the challenges of viral evolution. Like SARS-CoV-2, influenza viruses can evolve quickly. As such, current influenza vaccines must be reformulated annually in anticipation of the changing viral strains predicted to circulate during the upcoming influenza season. In the hopes of one day eliminating the need for annual vaccination, universal flu vaccines are being developed to generate long-lasting immune responses protective against many existing or emerging influenza strains. For example, NIAID scientists have begun clinical trials with an experimental universal flu vaccine, FluMos-v1. NIAID is investing in research to inform other vaccine approaches, such as a whole avian influenza virus cocktail, BPL-1357, as well as novel delivery mechanisms utilizing a new vector for a broadly protective intranasal vaccine and a vaccine targeting different influenza surface proteins than current vaccines do.

Pan-pathogen vaccines that protect against most variants of a pathogen are a promising strategy for vector-borne and parasitic diseases, where both vector and pathogen vary widely over time or across regions. For example, leishmaniasis is caused by a parasite carried by sandflies, but the subtypes of both the parasite and sandfly vary greatly across regions. Tick-borne diseases are similarly varied and increasingly prevalent in the United States. As a result of climate change, more people are at risk for contracting mosquito-borne diseases such as malaria, Zika, and West Nile. NIAID scientists are studying the mechanisms that enable mosquitoes, sandflies, and ticks to evade our immune system by masking the presence of pathogens. An examination of the role of proteins in the insect's saliva and the interactions between the vector, pathogen, and our immune system and microbiome is informing the development of broadly protective vaccine candidates for mosquito-borne diseases (see program portrait below), leishmaniasis, and tick-borne diseases. Broad protection provided by pan-pathogen vaccines may hinder the development of resistance to existing prevention and treatment approaches, and knowledge of the mechanisms involved will have further implications for other emerging and re-emerging pathogens.

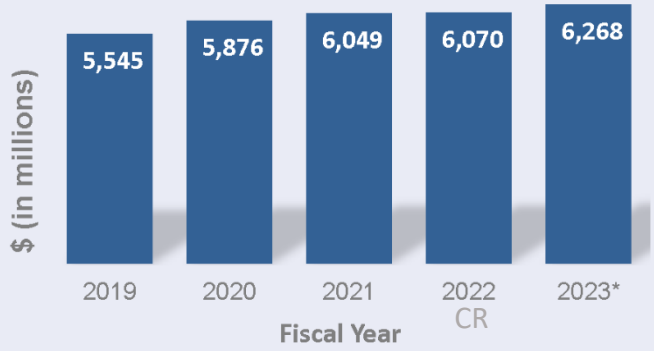
National Institute of Allergy and Infectious Diseases

ABOUT NIAID

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.

FUNDING HISTORY



*President's Budget request

FACTS AND FIGURES

1,976
FULL TIME EQUIVALENTS

1,305
FUNDED PRINCIPAL INVESTIGATORS

Averaged over FY18-FY21

RESEARCH HIGHLIGHTS

Pregnant people with COVID-19 are more likely to be severely ill than their non-pregnant peers. NIAID's MOMI-Vax trial is studying the immune responses elicited by vaccination of pregnant and postpartum people. The study will evaluate the transfer of vaccine-induced antibodies across the placenta and through breast milk to protect the infant.

NIAID launched the Adaptive COVID-19 Treatment Trial (ACTT) to evaluate promising therapeutics for treatment of adults hospitalized with COVID-19. The first study, ACTT-1, demonstrated the safety and efficacy of the antiviral, remdesivir, in shortening the time to recovery in hospitalized patients, resulting in FDA licensure.

Universal flu vaccines are being developed to generate long-lasting immune responses protective against many existing or emerging influenza strains. NIAID scientists have begun clinical trials with an experimental universal influenza vaccine, FluMos-v1. Participants will be followed over the 2021-2022 flu season to test its safety profile.

NIAID has an extensive program to develop adjuvants, ingredients in vaccines that boost immune responses and enhance a vaccine's effectiveness. Alhydroxiquim-II, an adjuvant developed with NIAID funding, was included as an essential component of COVAXIN, a COVID-19 vaccine developed in India and approved for use in 9 countries.

The microbiome holds promise to address antimicrobial resistance. NIAID researchers have identified signals sent between human host and microbiota that can affect antimicrobial defenses. An antimicrobial substance, micrococcin P1, found in skin microbiota, can reduce infection and accelerate wound healing in mice with MRSA infection.

National Institute of Allergy and Infectious Diseases

RESEARCH ADVANCES

To rapidly address the COVID-19 pandemic, NIAID built on many of the lessons learned from and expertise gained in responding to the HIV pandemic. Decades of NIAID-supported HIV research demonstrated the promise of monoclonal antibodies as treatment, prevention, and post-exposure prophylaxis, and several monoclonal antibodies have now been developed to prevent and treat COVID-19. NIAID leveraged HIV research expertise to rapidly launch critical clinical prevention trials, including successful mRNA vaccines for COVID-19. These vaccines are based on a detailed analysis of the viral protein structure, an approach also used in HIV research. Conversely, the mRNA vaccine technology proven effective for SARS-CoV-2 is now being applied to develop an HIV vaccine. The COVID-19 community, like the HIV research advocacy groups, has been involved in moving the research field forward, helping to identify key research questions, and developing approaches that meet the needs of diverse populations at high risk for COVID-19.

The emergence of infectious diseases continues to threaten the health of Americans. In the past two decades, three novel coronaviruses – severe acute respiratory syndrome (SARS) coronavirus, middle east respiratory syndrome (MERS) coronavirus, and SARS-CoV-2 – have caused major disease outbreaks. The 2020 global pandemic caused by SARS-CoV-2 underscores the devastation that this family of viruses can inflict and the critical need to develop vaccines that can protect against multiple coronavirus strains, including newly evolved viruses and variants. The aim of pan-coronavirus vaccines is to elicit protection against the coronaviruses we already know, such as SARS-CoV-2, and related coronaviruses that could potentially cause the next pandemic. NIAID established a multidisciplinary research program to design and advance pan-coronavirus vaccine candidates. These projects aim to assess the diversity and infectious potential of coronavirus family members and test vaccine approaches that can elicit strong and long-lasting immunity.

Mosquito-borne diseases are widespread and difficult to treat, with malaria having the greatest global impact. Currently only one vaccine with modest effectiveness is available for malaria prevention, underscoring the need for additional vaccine research. Two first-in-human clinical trials sponsored by NIAID show promise. A chemoprophylaxis vaccine approach, PfSPZ-CVac, combines live malaria parasites with one of two antimalarial drugs, pyrimethamine or chloroquine. Initial tests in humans suggest that higher doses of the vaccine-antimalarial drug combination were strongly protective. The second vaccine, AGS-v, elicits immune responses to mosquito saliva rather than any specific parasite, virus, or bacteria, and is intended to protect against a range of mosquito-transmitted diseases, such as Zika, malaria, West Nile fever, and dengue fever. A clinical trial of this vaccine was the first “universal mosquito vaccine” in humans and demonstrated that the vaccine is safe and can produce significant immune responses. Both vaccine candidates, if effective in larger clinical trials, could help protect against vector-borne diseases and help reverse stalled global progress against malaria and other mosquito-borne diseases.

Major Changes in the Fiscal Year 2023 President's Budget Request

Major changes by selected budget mechanism are briefly described below. The FY 2023 President's Budget request is $6,268.3 million, an increase of $198.7 million or 3.3 percent compared with the FY 2022 Continuing Resolution (CR) 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) (+$129.7 million; total $3,736.2 million):
NIAID will support a total of 5,496 Research Project Grant (RPG) awards in FY 2023. The increased funding will support research in NIAID's Biodefense and Emerging Infectious Diseases, Infectious and Immunologic Diseases, and HIV/AIDS program areas. Funding for competing RPGs is expected to increase by $131.6 million or 19.2 percent in FY 2023, while noncompeting RPG funding will decrease by $11.6 million or 0.4 percent. Overall RPG funding will increase by 3.6 percent.

Research and Development Contracts (+$62.8 million; total $1,054.7 million):
NIAID will continue to support trans-NIH initiatives, including ongoing cybersecurity efforts, as well as other HHS-wide initiatives.

Other Research (-$37.6 million; total $95.0 million):
NIAID will reduce Other Research funding, reflecting the completion of upgrades to existing facilities and building systems across 12 Regional Biocontainment Laboratories.

Intramural Research (+$25.8 million; total $818.7 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, influenza, antimicrobial resistance/combatting antibiotic-resistant bacteria (CARB), and tick-borne diseases. Funding will also support the proposed FY 2023 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 2021 Final		FY 2022 CR		FY 2023 President's Budget		FY 2023 +/- FY 2022 CR	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	3,574	$2,247,458	3,823	$2,729,400	3,723	$2,717,824	-100	-$11,576
Administrative Supplements	*(99)*	32,977	*(80)*	27,947	*(80)*	27,947	*(0)*	0
Competing:								
Renewal	215	538,452	185	239,378	209	271,409	24	32,031
New	1,366	651,084	1,102	446,126	1,292	545,520	190	99,395
Supplements	1	478	1	408	1	532	0	124
Subtotal, Competing	1,582	$1,190,014	1,288	$685,911	1,502	$817,461	214	$131,550
Subtotal, RPGs	5,156	$3,470,450	5,111	$3,443,257	5,225	$3,563,231	114	$119,974
SBIR/STTR	268	165,230	262	163,230	271	172,924	9	9,694
Research Project Grants	5,424	$3,635,680	5,373	$3,606,488	5,496	$3,736,155	123	$129,668
Research Centers:								
Specialized/Comprehensive	27	$78,096	27	$80,342	28	$82,993	1	$2,651
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	743	0	743	0	767	0	25
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	27	$78,838	27	$81,085	28	$83,760	1	$2,676
Other Research:								
Research Careers	317	$53,881	304	$54,129	320	$55,915	16	$1,786
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	232	0	232	0	240	0	8
Other	102	80,136	107	78,271	82	38,872	-25	-39,400
Other Research	419	$134,250	411	$132,632	402	$95,027	-9	-$37,606
Total Research Grants	5,870	$3,848,767	5,811	$3,820,205	5,926	$3,914,942	115	$94,738
Ruth L Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	272	$12,665	273	$12,843	278	$13,266	5	$424
Institutional Awards	904	52,458	911	53,192	931	54,948	20	1,755
Total Research Training	1,176	$65,123	1,184	$66,035	1,209	$68,214	25	$2,179
Research & Develop. Contracts	226	$965,164	242	$991,887	268	$1,054,724	26	$62,837
(SBIR/STTR) (non-add)	*(34)*	*(19,639)*	*(27)*	*(15,639)*	*(27)*	*(11,639)*	*(0)*	*(-4,000)*
Intramural Research	948	782,679	983	792,879	983	818,666	0	25,786
Res. Management & Support	1,130	387,116	1,197	398,613	1,197	411,767	0	13,154
SBIR Admin. (non-add)	*(0)*	*(806)*	*(0)*	*(1,600)*	*(0)*	*(1,600)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NIAID	2,078	$6,048,849	2,180	$6,069,619	2,180	$6,268,313	0	$198,694

[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, $6,268,313,000.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Summary of Changes

(Dollars in Thousands)

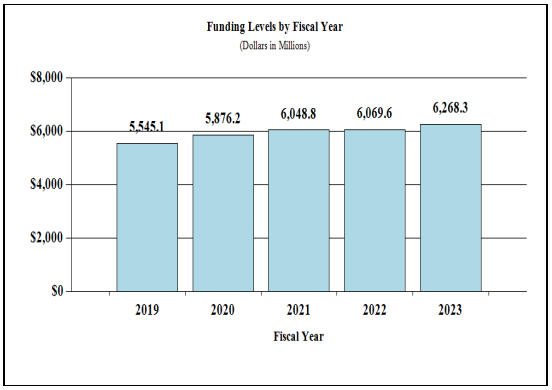
FY 2022 CR	$6,069,619
FY 2023 President's Budget	$6,268,313
Net change	$198,694

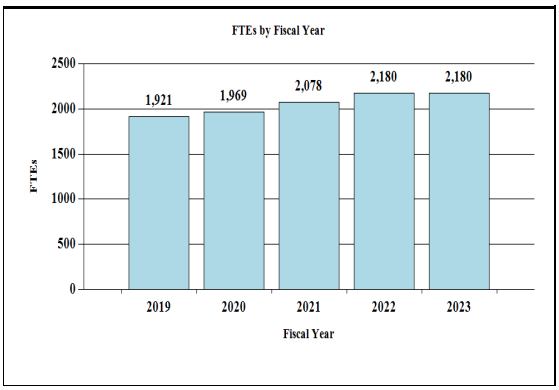
CHANGES	FY 2022 CR FTEs	FY 2022 CR Budget Authority	FY 2023 President's Budget FTEs	FY 2023 President's Budget Budget Authority	Built-In Change from FY 2022 CR FTEs	Built-In Change from FY 2022 CR Budget Authority
A. Built-in:						
1. Intramural Research:						
a. Annualization of January 2022 pay increase & benefits		$212,949		$224,348		$1,412
b. January FY 2023 pay increase & benefits		212,949		224,348		7,209
c. Paid days adjustment		212,949		224,348		-809
d. Differences attributable to change in FTE		212,949		224,348		0
e. Payment for centrally furnished services		109,776		111,971		2,196
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		470,154		482,347		10,196
Subtotal						$20,203
2. Research Management and Support:						
a. Annualization of January 2022 pay increase & benefits		$221,405		$230,341		$1,466
b. January FY 2023 pay increase & benefits		221,405		230,341		7,487
c. Paid days adjustment		221,405		230,341		-841
d. Differences attributable to change in FTE		221,405		230,341		0
e. Payment for centrally furnished services		31,124		31,746		622
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		146,084		149,680		3,105
Subtotal						$11,839
Subtotal, Built-in						$32,042

CHANGES	FY 2022 CR No.	FY 2022 CR Amount	FY 2023 President's Budget No.	FY 2023 President's Budget Amount	Program Change from FY 2022 CR No.	Program Change from FY 2022 CR Amount
B. Program:						
1. Research Project Grants:						
a. Noncompeting	3,823	$2,757,347	3,723	$2,745,771	-100	-$11,576
b. Competing	1,288	685,911	1,502	817,461	214	131,550
c. SBIR/STTR	262	163,230	271	172,924	9	9,694
Subtotal, RPGs	5,373	$3,606,488	5,496	$3,736,155	123	$129,668
2. Research Centers	27	$81,085	28	$83,760	1	$2,676
3. Other Research	411	132,632	402	95,027	-9	-37,606
4. Research Training	1,184	66,035	1,209	68,214	25	2,179
5. Research and development contracts	242	991,887	268	1,054,724	26	62,837
Subtotal, Extramural		$4,878,127		$5,037,880		$159,753
	FTEs		FTEs		FTEs	
6. Intramural Research	983	$792,879	983	$818,666	0	$5,583
7. Research Management and Support	1,197	398,613	1,197	411,767	0	1,315
8. Construction		0		0		0
9. Buildings and Facilities		0		0		0
Subtotal, Program	2,180	$6,069,619	2,180	$6,268,313	0	$166,652
Total built-in and program changes						$198,694

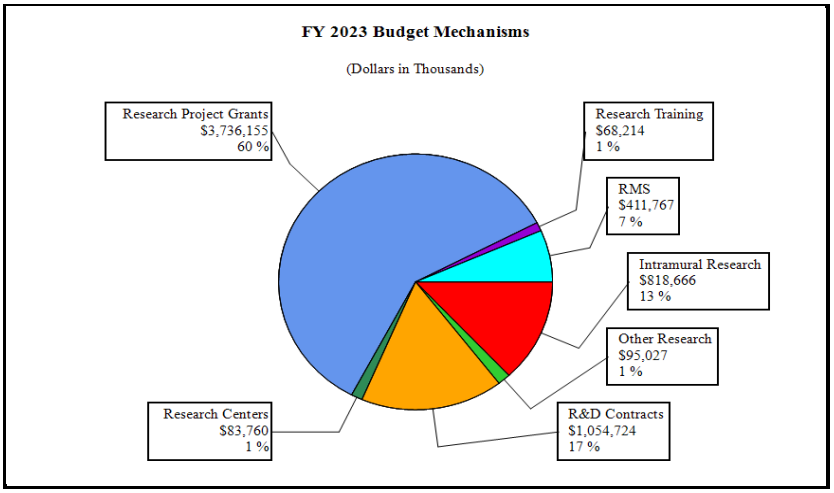
Fiscal Year 2023 Budget Graphs

History of Budget Authority and FTEs:

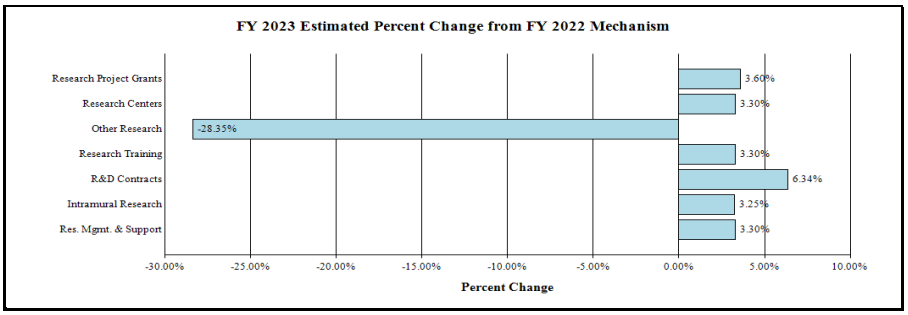




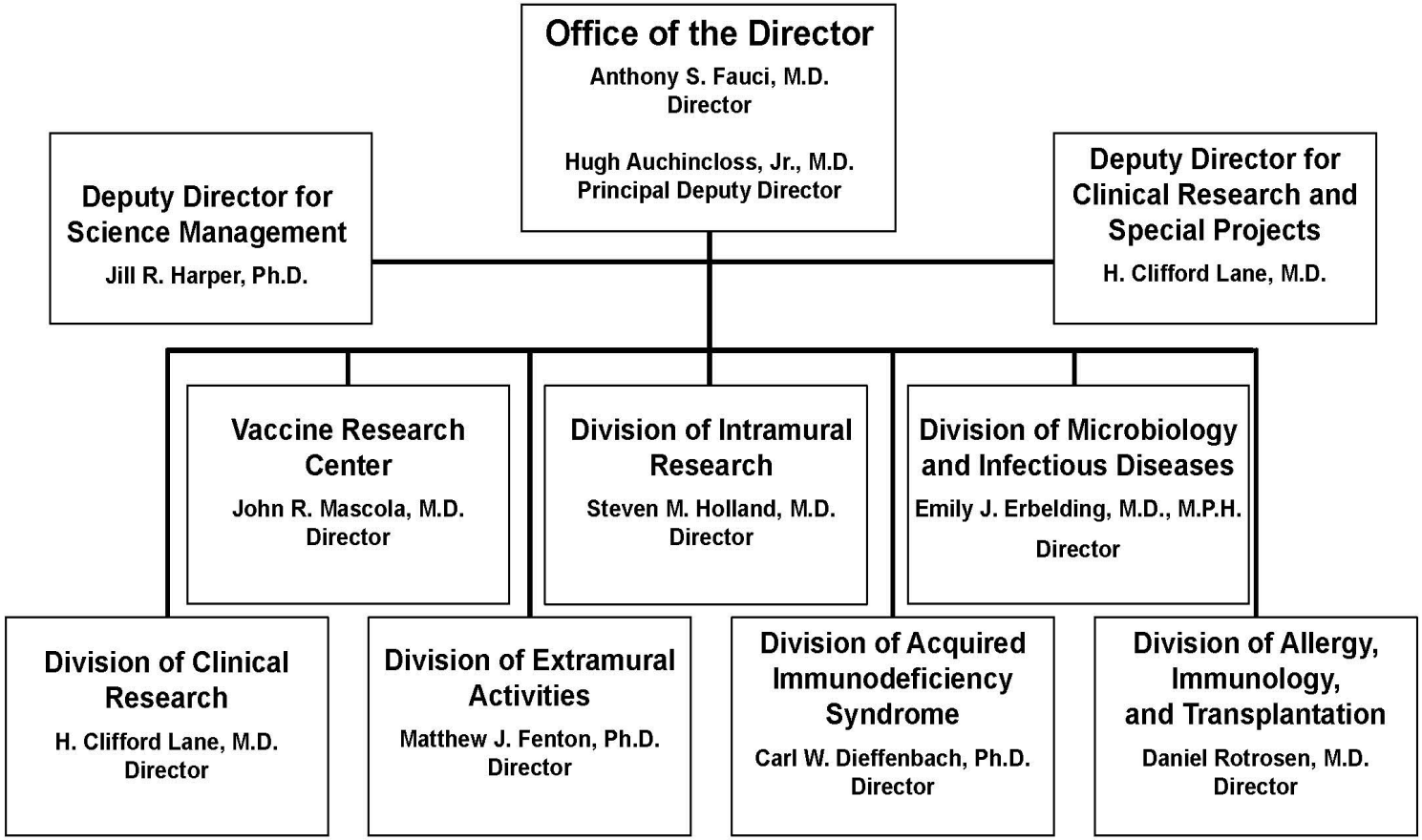
Distribution by Mechanism:



Change by Selected Mechanisms:



National Institutes of Health
National Institute of Allergy and Infectious Diseases
Organizational Structure



NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Budget Authority by Activity[1]

(Dollars in Thousands)

	FY 2021 Final		FY 2022 CR		FY 2023 President's Budget		FY 2023 +/- FY 2022 CR	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
HIV/AIDS [2]		$1,433,521		$1,437,588		$1,434,426		-$3,162
Biodefense & Emerging Infectious Diseases [3]		2,016,196		2,018,663		2,130,912		112,248
Infectious & Immunological Diseases		1,429,338		1,421,876		1,472,543		50,667
Subtotal, Extramural		**$4,879,054**		**$4,878,127**		**$5,037,880**		**$159,753**
Intramural Research	**948**	**$782,679**	**983**	**$792,879**	**983**	**$818,666**	**0**	**$25,786**
Research Management & Support	**1,130**	**$387,116**	**1,197**	**$398,613**	**1,197**	**$411,767**	**0**	**$13,154**
TOTAL	**2,078**	**$6,048,849**	**2,180**	**$6,069,619**	**2,180**	**$6,268,313**	**0**	**$198,694**

[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) $1,783,470 in FY 2021; $1,791,391 in FY 2022; and $1,798,843 in FY 2023.

[3] Reflects NIAID extramural total for Biodefense. NIAID-wide totals are (in thousands) $2,488,252 in FY 2021; $2,495,748 in FY 2022; and $2,622,309 in FY 2023.

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 2021 Final	FY 2022 CR	FY 2023 President's Budget	FY 2023 +/- FY 2022
BA	$6,048,849,000	$6,069,619,000	$6,268,313,000	+$198,694,000
FTE	2,078	2,180	2,180	0

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

Overall Budget Policy:
The FY 2023 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 importance of executing NIAID's dual mandate is underscored by the ongoing response to the COVID-19 pandemic.

The FY 2023 President's Budget request is $6,268.3 million, an increase of $198.7 million or 3.3 percent compared with the FY 2022 CR level. The Institute dedicates its annual resources to support biomedical research that aligns with its mission and addresses domestic and global health issues, such as the recent COVID-19 pandemic.

While NIAID continues to fund research to understand and develop medical countermeasures to address the COVID-19 pandemic, the Institute also remains focused on other high priority areas of research such as other emerging infectious diseases, agents with bioterrorism potential, HIV/AIDS, influenza, tuberculosis, malaria, drug-resistant microbes, tick-borne diseases, autoimmune disorders, asthma, and allergies. In FY 2023, 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 opportunities provided to established investigators who submit new R01 applications.

The FY 2023 request includes specific increases over the FY 2022 CR level, which include $40.0 million to continue efforts to develop a universal influenza vaccine, $20.0 million for

health disparities research, and $10.0 million to support the *Ending the HIV Epidemic in the U.S.* (EHE) initiative[1]. The request also continues 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 research on CARB and tick-borne diseases.

Program Descriptions

HIV/AIDS

Decades of basic 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) do not 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 vulnerable to HIV. Despite this progress, an estimated 1.2 million Americans were living with HIV in 2020, although 13 percent of them were aware of their HIV status. While an end to the HIV epidemic is theoretically possible, it will require new prevention approaches and treatments that must be refined, developed, and tested.

A universal test and treat approach—testing all members of a community and treating anyone with HIV to improve their health and prevent transmission—has proven very effective at decreasing HIV spread in areas with high levels of HIV. Despite overall efficacy, a subset of people still have unsuppressed virus. A recent NIAID study showed that these people tended to be younger, male, and mobile. Knowing this can inform strategies targeted at reducing the stigma of HIV that may lead to suboptimal prevention and treatment in these populations.

NIAID-supported investigators have been working to develop a long-acting alternative to oral PrEP that would be more desirable than taking a daily pill. Two clinical trials recently showed that the long-acting injectable drug cabotegravir outperformed daily PrEP in men and transgender women who have sex with men, as well as in cisgender women in Africa. The U.S. Food and Drug Administration (FDA) has moved this intervention to fast-track approval. Earlier NIAID trials had shown that a vaginal ring containing the drug dapivirine could protect women from acquiring HIV. Following its approval by the European Medicines Agency and a recommendation from the World Health Organization (WHO), some countries in Africa are starting to approve it for use, providing a convenient and discreet option for women to complement other prevention tools.

The development of a safe and effective HIV vaccine has proven to be a formidable scientific challenge. In addition to attacking the immune system, HIV mutates rapidly and has many strains. One approach to vaccine development is the identification of novel immunogens,

[1] Details on the **PrEP Delivery Program** to End the HIV Epidemic are included in the Mandatory Proposals section of the Departmental Management Congressional Justification.

proteins that elicit an immune response. Two studies were launched to examine an investigational vaccine based on "mosaic" immunogens—vaccine components comprising elements from multiple HIV subtypes. An interim analysis of the trial examining the mosaic vaccine in women recently found the vaccine to be safe but not sufficiently effective at protecting women from HIV. However, the trial in transgender women and men who have sex with men is ongoing. Another HIV vaccine strategy involves harnessing the potential of broadly neutralizing antibodies (bNAbs), which, laboratory studies indicate, can prevent a wide variety of HIV strains from infecting cells. Results reported in January 2021 from the AMP (Antibody-Mediated Protection) studies demonstrated that passive administration of a bNAb can prevent a person from acquiring HIV strains susceptible to that antibody. Currently, early-stage clinical trials are testing several next-generation bNAbs, individually and in combination, for HIV prevention. In parallel, scientists are working to develop candidate vaccines that can elicit bNAbs in healthy people.

ART can suppress viral load to undetectable and untransmittable levels; however, this requires regular monitoring, and viral levels can rebound if treatment is stopped. NIAID supports substantial efforts to develop better treatments, including bNabs. Multiple bNAbs are being developed, including N6LS, which was first tested by NIAID scientists and is now being advanced for clinical use by a company. Unfortunately, HIV resistance to bNAbs (i.e., continued viral replication despite the presence of bNAbs) can emerge during treatment. NIAID is seeking to better understand how resistance emerges and if different combinations of bNAbs can alleviate this phenomenon. For example, resistance may result from pre-existing bNAb-resistant viruses, or from the *de novo* evolution of newly resistant viruses during bNAb treatment. These results will help identify optimal bNAbs combinations for therapeutic use.

To accelerate HIV cure research, NIAID expanded its Martin Delaney Collaboratories for HIV Cure Research program, including a new Collaboratory specifically focused on developing a pediatric cure. A variety of concepts are being examined by the Collaboratories, including exploring compounds to either flush out latent HIV or prevent its activation, inhibit latency establishment upon starting ART, studying correlates of control of HIV rebound, and using genetically engineered viruses to identify viral reservoirs. New therapeutic technologies include engineering immune cells to express broadly neutralizing antibodies, mRNA vaccines, and nanoparticle vaccines. Another important new concept is the use of gene therapy for a cure. Gene-editing technology could be used to inactivate or remove dormant HIV, enhance immune responses, and engineer immune cells to be resistant to HIV infection. In collaboration with the Bill & Melinda Gates Foundation, NIAID is stimulating research into new technologies for anti-HIV gene therapy that could one day replace the need for ART.

SYNERGISTIC IMPACT OF HIV RESEARCH ON COVID-19 RESPONSE

To rapidly address the COVID-19 pandemic, NIAID built on many of the lessons learned from responding to the HIV pandemic. Four decades of NIAID-supported HIV research demonstrated the promise of monoclonal antibodies as treatment, prevention, and post-exposure prophylaxis, and several monoclonal antibodies have now been developed to treat and prevent COVID-19. Similarly, the search for effective antivirals to treat COVID-19 is modelled on the success of HIV antivirals.

New technologies have evolved over the last decade driven largely from efforts to develop an HIV vaccine. In 2020, NIAID leveraged HIV research expertise to rapidly launch critical clinical prevention trials, including the successful mRNA vaccines for COVID-19. Conversely, the mRNA vaccine technology that proved effective for SARS-CoV-2 is now being applied to develop a candidate HIV vaccine. NIAID also leveraged existing HIV research infrastructure, merging four HIV and infectious disease clinical trials networks to create the COVID-19 Prevention Network (CoVPN). The CoVPN rapidly enrolled more than 90,000 volunteers in trials while ensuring diverse populations were represented in these studies. While answering the call to test COVID-19 vaccines and therapeutics, these networks continued to perform clinical trials and test prevention strategies for HIV and other infectious diseases.

People with HIV are also at high risk for severe COVID-19, highlighting the importance of community interaction and education to foster trust and uptake of vaccines, therapeutics, and preventive strategies for both COVID and HIV.

Budget Policy:
The FY 2023 President's Budget request for the extramural component of the HIV/AIDS research is $1,434.4 million, a decrease of $3.2 million or 0.2 percent compared with the FY 2022 CR level. NIAID will continue to support basic, translational, and clinical research aimed at reducing incidence of infection. Research priorities will focus on development of an effective vaccine and biomedical prevention strategies, development of novel approaches for the treatment and cure of HIV infection, and development of interventions to treat and/or prevent co-infections and co-morbidities. The FY 2023 request includes $10.0 million of additional funding over the FY 2022 CR level for the EHE initiative to expand implementation research activities conducted by CFARs and ARCs.

Biodefense and Emerging Infectious Diseases
The COVID-19 pandemic has reminded us of the global havoc that can be caused by an emerging infectious disease. As part of NIAID's mandate to respond rapidly to emerging disease threats and outbreaks, NIAID developed the *NIAID Strategic Plan for COVID-19 Research* in 2020 and updated it in 2021 to coordinate research efforts on fundamental research on SARS-CoV-2, diagnostics, therapeutics, vaccines, and the long-term effects of infection.

To rapidly test therapeutics and vaccines against COVID-19, NIH, with significant NIAID participation, developed an unprecedented public-private partnership called Accelerating COVID-19 Therapeutics and Vaccines (ACTIV). Since its establishment, 25 therapeutic agents have been prioritized for testing in rigorous clinical trials for COVID-19 patients in both inpatient and outpatient trials. The results of the ACTIV clinical trials are reflected in regular updates to the NIH COVID-19 Treatment Guidelines.

In addition, NIAID launched the Adaptive COVID-19 Treatment Trial (ACTT) to evaluate promising therapeutics for treating adults hospitalized with COVID-19. The adaptive nature of ACTT enabled NIAID to rapidly launch trials. The first study, ACTT-1, demonstrated the safety and efficacy of the antiviral remdesivir in shortening the time to recovery in hospitalized patients, resulting in FDA licensure. ACTT-2 improved on those results, showing the additional benefit of baricitinib, a drug designed to reduce inflammation, for hospitalized patients receiving remdesivir. The FDA subsequently issued an Emergency Use Authorization (EUA) for the combination of baricitinib and remdesivir for treating hospitalized patients with COVID-19. To continue efforts to develop safe and effective antivirals to combat SARS-CoV-2, NIAID, in conjunction with other NIH Institutes and Centers, launched the Antiviral Program for Pandemics (APP). In 2022, as part of the APP, NIAID will establish Antiviral Drug Discovery (AViDD) Centers for Pathogens of Pandemic Concern. These multidisciplinary research centers will create platforms that will target coronaviruses and one or more additional RNA viruses with

pandemic potential – helping to better prepare the nation for future viral threats. Oral drug candidates for broad use in outpatient settings are the primary focus of this effort.

Even though several effective vaccines against COVID-19 are now available, additional studies are needed to maximize their real-world utility. One priority is understanding the safety and effectiveness of employing heterologous prime-boost strategies, that is using different combinations of COVID vaccines for the prime and booster doses. NIAID completed a trial that demonstrated the safety and efficacy of such an approach and the FDA approved the use of heterologous or 'mix and match' booster doses in October 2021. After reports of severe allergic reactions to the mRNA vaccines surfaced, NIAID quickly responded by launching a Phase 2 trial to examine whether people with allergies or certain immune disorders are at increased risk for severe allergic reactions like anaphylaxis. A complementary study was launched at the NIH Clinical Center to assess the safety of a second dose in patients who had an allergic reaction to the first dose with the goal of determining the mechanisms underlying these reactions.

PAN-CORONAVIRUS VACCINES

The emergence and re-emergence of infectious diseases continues to threaten the health of Americans and people worldwide. In the past two decades, three novel coronaviruses – SARS-CoV-1, MERS-CoV, and most recently SARS-CoV-2 – have caused major disease outbreaks. The 2020 global pandemic caused by SARS-CoV-2 underscores the devastation that this family of viruses can inflict and the critical need to develop vaccines capable of broad protection against multiple coronavirus strains, including newly emerging viruses and variants. The aim of pan-coronavirus vaccines is to elicit protection against the coronaviruses we already know, such as SARS-CoV-2, and related coronaviruses that could potentially cause the next pandemic. To that end, NIAID established a multidisciplinary research program specifically to design and advance pan-coronavirus vaccine candidates. These projects aim to assess the diversity and infectious potential of coronavirus family members, test vaccine approaches that can elicit strong and long-lasting pan-coronavirus immunity and evaluate pan-coronavirus vaccine candidates in cellular and animal models. Such an approach builds on pre-clinical success seen with the development of experimental pan-influenza vaccines, BPL-1357 and FluMos-v1. NIAID is exploring the development of pan-pathogen vaccines for other diseases as well (see Director's Overview and IID Program Portrait). Developing successful pan-pathogen vaccines could prevent a disease outbreak from becoming the next pandemic.

To ensure that all people benefit from COVID-19 vaccination, NIAID supports clinical trials in special populations such as pregnant and immunocompromised people. Pregnant people infected with COVID-19 are more likely to be hospitalized and severely ill than their non-pregnant peers. The MOMI-Vax study is characterizing the immune responses elicited by vaccination of pregnant and postpartum people. The study will evaluate the transfer of vaccine-induced antibodies across the placenta and through breast milk to protect the infant. NIAID researchers are comparing immune system responses to COVID-19 vaccines in people with and without immune deficiencies to gain a comprehensive understanding of the variety of immune responses to these vaccines. In another study, NIAID researchers are evaluating an extra vaccine dose in kidney transplant recipients who did not develop protective antibodies after two doses of either the Moderna or Pfizer-BioNTech mRNA vaccines. Like transplant recipients, people with autoimmune diseases take medication to suppress their immune systems, and as such, may require an extra vaccine dose.

To examine this question, NIAID-supported researchers are administering an extra vaccine dose to people with one of five autoimmune diseases: multiple sclerosis, pemphigus, rheumatoid arthritis, systemic lupus erythematosus, or systemic sclerosis. Some of the subjects will discontinue their immune-suppression medication for a short period before and after receiving an extra dose to see if this will elicit better antibody production. Finally, NIAID is collaborating with Moderna to utilize the Vaccine and Treatment Evaluation Units (VTEUs) for the KidCOVE study, which is evaluating 3 different doses of the Moderna mRNA-1273 vaccine in healthy children 6 months to less than 12 years of age.

To support the development of effective vaccines against many diseases, NIAID has an extensive program to develop adjuvants, ingredients in vaccines that boost immune responses and enhance a vaccine's effectiveness. For example, alhydroxiquim-II, an adjuvant developed with NIAID funding, was included as an essential component of COVAXIN, a COVID-19 vaccine developed in India. COVAXIN is currently approved for use in 9 countries.

NIAID also rapidly launched cohort studies that use cutting-edge approaches to better understand the immune response to SARS-CoV-2 infection. The Immunophenotype Assessment in a COVID-19 Cohort (IMPACC) study is collecting clinical samples from adults hospitalized with COVID-19 for detailed analysis of various aspects of the human immune response to the virus. This knowledge will lead to a better understanding of how this disease affects people, including risk factors for disease severity and long-COVID complications, and to optimal treatment strategies. Additionally, the Human Epidemiology and Response to SARS-CoV-2 (HEROS) study followed children and their families for six months to determine who became infected with SARS-CoV-2, whether the virus was transmitted to other household members, and which household members with the virus developed COVID-19. NIAID also is participating in RECOVER (Researching COVID to Enhance Recovery), a large NIH effort to delineate and characterize the long-term impacts of Post-Acute Sequelae of SARS-CoV-2 (PASC), including long-COVID, in both children and adults (see more in the Crosscutting Initiatives section of the NIH Congressional Justification Overview volume).

In addition to responding to the global COVID-19 pandemic, NIAID has responded to several Ebola virus disease (EVD) outbreaks by mobilizing its flexible infrastructure and collaborating through established clinical research partnerships. One such research collaboration, the PALM (Pamoja Tulinde Maisha) trial, resulted in FDA approval of two monoclonal antibody (mAb) treatments for EVD – Inmazeb and Ebanga. The mAb that comprises Ebanga was first isolated from an EVD survivor by NIAID scientists. To limit and stop EVD outbreaks, NIAID also is investing in the development of EVD vaccines. NIAID leads the Partnership for Research on Ebola Vaccination (PREVAC), a research collaboration testing three different vaccine strategies to prevent EVD in children and adults. Separate, ongoing clinical trials are examining the safety of two additional vaccine candidates for EVD and Marburg, a disease caused by a close viral relative of Ebola. Both use the vaccine vector cAd3, a delivery system developed by NIAID scientists and are currently being advanced by the Sabin Vaccine Institute. To mitigate EVD spread, NIAID scientists developed two new rapid diagnostic tests. One recognizes certain

Ebola virus proteins in the blood only four days after infection. The other is a portable field assay that tests for Ebola virus in wildlife carcasses to rapidly identify possible new outbreaks.

Resistance to antibiotics and other antimicrobial drugs is also a growing public health concern, causing 2.8 million infections and 35,000 deaths in the United States each year.[2] Antimicrobial resistance occurs when pathogens change over time and no longer respond to treatment. NIAID continues to make significant investments into basic, translational, and clinical research on antimicrobial resistance, including supporting the government-wide National Action Plan for Combatting Antibiotic-Resistant Bacteria (CARB). NIAID works to identify promising countermeasures to accelerate the fight against antimicrobial resistance and works closely with the Biomedical Advanced Research and Development Authority (BARDA) to further develop them. NIAID and BARDA supported the Antimicrobial Resistance Diagnostic Challenge to develop innovative, rapid, point-of-care diagnostics that identify drug-resistant pathogens and treatment strategies. Such targeted treatment approaches reduce the risk of developing drug resistance. The test that won this challenge can diagnose gonorrhea and determine the best treatment in less than 30 minutes.

In FY 2020, NIAID established several new programs related to antimicrobial resistance, including the Chemistry Center for Combatting Antibiotic-Resistant Bacteria (CC4CARB), to design, synthesize and deliver novel compounds to the scientific community; and the Combatting Antibiotic-Resistant Bacteria Interdisciplinary Research Units (CARBIRUs) which are exploring bacterial and human factors that influence drug resistance. NIAID also renewed the Antibacterial Research Leadership Group (ARLG), which designs and implements the clinical research agenda to address antibacterial resistance. ARLG advances research by developing transformational clinical trials that aim to change clinical practice and reduce the impact of antibacterial resistance. For example, a recent ARLG study of community-acquired pneumonia in children showed that a 5-day antibiotic course was better than the standard 10-day treatment, reducing both side effects and the risk of antibiotic resistance.

Bacteriophages, or phages, also can be used to treat antibiotic resistant infections. These viruses directly infect and destroy bacteria, bypassing bacterial antibiotic resistance mechanisms. NIAID scientists tested phage therapy in mice infected with multidrug-resistant *Klebsiella pneumoniae*, a bacterium that can lead to pneumonia, bloodstream infections, meningitis, or urinary tract infections. When treated with either of two different phages, P1 or P2, all mice recovered from *K. pneumoniae* infection. In 2021, NIAID prioritized this area of research, funding its first set of projects to address key knowledge gaps in the development of phages as preventative and therapeutic tools for bacterial infections. ARLG scientists will also test a bacteriophage cocktail for the treatment of cystic fibrosis patients with treatment-resistant *Pseudomonas aeruginosa* infections.

The spread of drug resistance is also an ongoing concern for tuberculosis (TB), which remains the leading cause of death among infectious diseases and one of the top 10 causes of death

[2] cdc.gov/drugresistance/index.html

worldwide. In a recent clinical trial, investigators showed that a 4-month drug treatment regimen was as efficient as the standard 6-month regimen, with fewer side effects, and less risk of drug resistance, while allowing for better patient adherence to treatment. In collaboration with private-sector partners, the PredictTB program is evaluating markers of disease in patients with drug-sensitive TB to determine if they could benefit from a shorter treatment course. To prevent the spread of multidrug resistant-TB in households, NIAID's Protecting Households On Exposure to Newly Diagnosed Index trial is testing whether the anti-TB drug delamanid is better than the standard isoniazid treatment for preventing TB disease in at-risk household members. Additionally, NIAID is evaluating how anti-TB drugs are absorbed, distributed, and metabolized in the body during and after pregnancy to better understand how best to treat pregnant people without harming their fetuses. To characterize immune responses to TB, NIAID launched IMPAc-TB in FY 2019. Results from the program have identified early immune responses that predict the ability to control the infection, which are helping to inform new candidate vaccines and treatments.

Vaccines that either prevent infection or transition to active TB are urgently needed to decrease the global burden of TB. A NIAID initiative, the Innovation in TB Vaccine Discovery, emphasizes high risk/high impact strategies for vaccine design that incorporate novel technologies. NIAID is supporting the comparison of different adjuvants in combination with tuberculosis immunogens to develop effective vaccines. Finally, NIAID is establishing Tuberculosis Research Advancement Centers to foster multidisciplinary TB research, mentor new TB investigators, and strengthen TB clinical research whether related to vaccines or treatment. Ending the TB pandemic will depend on identifying the millions of individuals with TB who are undiagnosed. NIAID launched Feasibility of Novel Diagnostics for TB in Endemic Countries (FEND for TB) in 2020, to evaluate and improve TB diagnostics for both drug-susceptible and drug-resistant TB with a special emphasis on diagnostics for point of care settings as well as in children and adults with HIV.

NIAID is committed to addressing the threat to public health posed by the rising incidence of tickborne diseases (TBDs), such as Lyme disease, in the United States. Current strategies to address TBDs are hindered by suboptimal diagnostics, a paucity of treatment options for viral and other TBDs, and a lack of vaccines. The NIH Strategic Plan for Tickborne Disease Research proposes additional research to better understand the complex interplay among host, tick, and pathogen factors that contribute to TBDs and the body's defenses against them. NIAID will leverage this knowledge to develop new tools to effectively prevent, diagnose, and treat TBDs for all stages of disease and across diverse populations and age groups.

Budget Policy:
The FY 2023 President's Budget request for the extramural component of Biodefense and Emerging Infectious Diseases research supported by NIAID is $2,130.9 million, an increase of $112.2 million or 5.6 percent compared with the FY 2022 CR level. NIAID will continue to conduct and support research to better understand, prevent, and treat infectious diseases of public health concern.

The FY 2023 request will also support the development of medical countermeasures and new platform technologies as part of a strategy to address emerging and re-emerging infectious disease pathogens. An increase of $40.0 million over the FY 2022 CR level will support NIAID efforts to continue 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. 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, and will also support development of therapeutics against antibiotic-resistant bacteria.

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. Support for collaborative, multidisciplinary research on developing vaccines for STIs, identifying immune cells that drive celiac disease, addressing endemic fungal disease such as Valley fever, and advancing research on hepatitis B and C viruses will begin to address the magnitude of burden imposed by these diseases.

The prevalence of food allergy among children under 18 has been increasing. NIAID researchers have identified several risk factors for developing food allergy, but the reasons food allergy has been increasing remain unknown. Allergic reactions to foods can range from mild, such as gastrointestinal symptoms or skin rashes, to severe, including the life-threatening allergic reaction called anaphylaxis. In March 2021, NIAID launched the observational Systems Biology of Early Atopy, or SUNBEAM study to identify prenatal and early childhood biomarkers of high risk for the development of food allergy and atopic dermatitis, as well as biological pathways that lead to these conditions. The study is enrolling children from birth to age three and will examine the roles and interrelationships between clinical, environmental, biologic, and genetic factors in the development of allergic diseases. Results from the study will help guide the implementation of current prevention strategies and facilitate new approaches to the prevention and treatment of food allergy.

Atopic dermatitis, or eczema, is a chronic inflammatory skin disease characterized by dry, itchy skin and rashes. Most common in children, atopic dermatitis increases the risk of developing asthma, hay fever, and food allergy and can require costly and cumbersome treatments. In addition to the SUNBEAM study, NIAID researchers are exploring the numerous genetic and environmental factors that contribute to eczema, including the role of the skin's microbiota—the community of bacteria and other microbes living on the skin. NIAID investigators found that treatment with *Roseomonas mucosa*, a bacterium of the skin's microbiota, can safely reduce eczema disease severity and increase quality of life. Additionally, new research supported by NIAID has delineated how two relatively common variations of a gene called *KIF3A* impair skin barrier function, leading to increased water loss and the potential development of eczema. With

the identification of these gene variations, infants could be screened for them potentially. Furthermore, therapies addressing water loss from the skin might prevent eczema in these children, thereby preventing a cascade of additional allergic diseases later in life.

More than 25 million people in the United States have asthma, including 5.1 million children.[3] This chronic lung disease can reduce quality of life, and severe asthma attacks can be life-threatening and lead to numerous emergency room visits and hospitalizations. In 2021, NIAID supported the establishment of the Childhood Asthma in Urban Settings (CAUSE) network. This nationwide network will conduct observational studies and clinical trials to improve the understanding of asthma and develop treatment and prevention approaches tailored to children of low-income families living in urban communities. This initiative extends and expands NIAID's long-standing efforts to better understand and address health disparities in asthma prevalence and treatment.

Respiratory syncytial virus (RSV) infection in infants hospitalized with bronchiolitis, a severe childhood lung infection, is the most impactful risk factor for developing asthma later in childhood. Recently, the MARC-35 (35th Multicenter Airway Research Collaboration) study identified which infants hospitalized with RSV were at highest risk for developing asthma by age five. These findings will be expanded to help target prevention strategies. RSV vaccine candidates based on vaccine prototypes developed by NIAID scientists are in advanced development by industry. Another clinical trial, Preventing Asthma in high-Risk Kids (PARK), is evaluating whether blocking IgE, an antibody critical in the development of allergies

MALARIA AND MOSQUITO VACCINES

Mosquito-borne diseases are widespread and difficult to treat, with malaria having the greatest global impact. Roughly 3.2 billion people—almost half the world's population—are at risk of malaria and there is a pressing need for a highly effective malaria vaccine. NIAID supported two recent clinical trials for vaccines that have shown promising protection against malaria.

In collaboration with a small business, NIAID scientists developed a chemoprophylaxis vaccination (PfSPZ-CVac) approach that combines vaccination with live parasites and one of two antimalarial drugs, pyrimethamine or chloroquine. Initial tests in humans suggest that higher doses of the vaccine-antimalarial drug combination had very strong protective results; the combination with chloroquine showed a remarkable 100 percent protection. Larger Phase 2 studies are currently under development and, if successful, suggest that chemoprophylaxis vaccination could be a promising preventative strategy for those living in or traveling to endemic areas.

NIAID scientists also developed another vaccine, Anopheles gambiae saliva vaccine (AGS-v), which elicits an immune response to mosquito-derived substances rather than any specific parasite, virus, or bacteria. Instead of targeting the pathogen itself, the AGS-v vaccine elicited immune responses against four mosquito salivary proteins. In animal models, immunity to mosquito salivary proteins protected animals from many different mosquito-borne diseases. A clinical trial of this vaccine was the first "universal mosquito vaccine" in humans and demonstrated that the vaccine is safe and produced significant immune responses. Both the PfSPZ-CVac and AGS-v candidates, if shown to be effective in larger clinical trials, could help reverse stalled global progress against malaria.

[3] cdc.gov/vitalsigns/asthma/index.html

and asthma, can prevent asthma in high-risk children ages 2-4 years old. The PARK trial results will advance our understanding of the pathogenesis, treatment, and prevention of asthma.

Many mutations in immune system genes affect the development and function of infection-fighting immune cells, causing rare immune deficiencies such as severe combined immunodeficiency (SCID). This condition is fatal, usually within the first two years of life, unless the infants' immune system is restored by a transplant of blood-forming stem cells, gene therapy, or enzyme therapy. The SCID newborn screening test, originally developed at NIH, has made it possible to detect SCID before symptoms appear, helping ensure that affected infants receive life-saving treatments. NIAID researchers have now developed an investigational gene therapy that safely restores the immune systems of infants and children who have one version of this rare, life-threatening disorder. XMEN disease, another disorder of the immune system, was first described by NIAID investigators in 2011 and is characterized by low levels of infection-fighting immune cells. Existing treatment options are associated with high mortality, so alternative therapeutic options are needed. Using gene editing technology, NIAID researchers were able to genetically alter the cells in mice responsible for creating new immune cells, fix the mouse counterpart of the defective gene associated with XMEN disease, and restore cellular function. This treatment approach is now poised for testing in humans with XMEN disease.

Sexually transmitted infections are an important global health priority because of their devastating impact on women and infants and their interrelationships with HIV/AIDS. Infection with certain STIs can increase the risk of getting and transmitting HIV as well as alter the way the disease progresses. When left untreated, STIs can cause long-term health problems including infertility and neurological impairments. Cases of syphilis, gonorrhea, and chlamydia have increased in the United States. NIAID established four STI Cooperative Research Centers to advance the development of vaccines against the pathogens that cause these STIs.

Malaria, a mosquito-borne disease caused by *Plasmodium* parasites, remains a major global public health problem and an important topic of NIAID research (see Program Portrait). In a first-in-human study, NIAID researchers have evidence that one dose of an antimalarial monoclonal antibody (mAb) can prevent infection. Researchers at NIAID discovered and isolated a mAb against malaria from a volunteer who received an investigational malaria vaccine and then modified it to extend the amount of time the mAb would remain in the bloodstream, creating mAb CIS43LS. In a Phase 1 clinical trial, one dose of CIS43LS was safe and prevented malaria in a controlled human challenge up to nine months after administration. A larger Phase 2 clinical trial is underway in Mali—where malaria is endemic—to evaluate the safety and efficacy of this mAb at preventing malaria infection in adults.

Budget Policy:

The FY 2023 President's Budget request for the extramural component of Infectious and Immunologic Diseases research is $1,472.5 million, an increase of $50.7 million or 3.6 percent compared with the FY 2022 CR level. NIAID will continue to advance long-range research priorities in infectious and immunologic diseases. The FY 2023 request will support NIAID's commitment and long-term interest in fundamental immunology, as well as research on malaria,

neglected tropical diseases, hepatitis, TB, sexually transmitted infections (STIs), fungal diseases, autoimmune diseases, organ transplantation, asthma, and allergic diseases.

Intramural Research Program (IRP)

The NIAID Intramural Research Program (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 (DIR), 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 research 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 domestic and international partnerships, allows NIAID to execute high-risk and long-term studies, conduct research on rare diseases, and rapidly respond to global public health emergencies.

A recent collaboration between DIR and academic researchers identified a mechanism where organisms living in or on our body surfaces—called the microbiota—communicate with each other and with the human immune system. Pieces of viruses that were previously infectious can integrate in the human host's DNA and influence how the host immune system and microbiota interact. This communication can affect tissue repair and antimicrobial defenses. In another highly collaborative study of the body's natural defenses against bacterial infection, NIAID IRP investigators along with researchers from four other NIH Institutes identified a nutrient—taurine—that helps the gut recall prior infections and kill invading bacteria, such as *Klebsiella pneumoniae*. This finding could aid efforts seeking alternatives to antibiotics and reduce antimicrobial resistance. Additionally, IRP researchers identified an antimicrobial substance called micrococcin P1 (MP1) found in a species of bacteria from the skin's microbiota. Topical application of MP1 reduced infection and accelerated healing of wounds in mice with methicillin-resistant *Staphylococcus aureus* infection.

Finally, the IRP plays an essential role in rapidly responding to public health emergencies across the globe. Intramural investigators created the mRNA for the stabilized SARS-CoV-2 spike protein within 3 days of the publication of the virus' genome, enabling the rapid generation and testing of a vaccine. NIAID scientists also conducted the first-in-human COVID-19 vaccine trial and provided scientific expertise and leadership for the U.S. Government's COVID-19 effort, including expert clinical trial and immunologic support for phase 3 clinical trials, such as assays that measure immune responses to COVID-19 vaccines. The pandemic response involved intense discussion and close collaborations with global entities such as the WHO, as well as coordination with many local and foreign governments. Similarly, NIAID staff members advised the Indian government in responding to the 2021 Nipah virus outbreak.

Budget Policy:
The FY 2023 President's Budget request for Intramural Research is $818.7 million, an increase of $25.8 million or 3.3 percent compared with the FY 2022 CR level. The FY 2023 Intramural Research plan supports NIAID's critical long-range research priorities with funding carefully aligned to support key research activities. These activities include continued support for all aspects of research on infectious diseases such as HIV/AIDS, malaria, and influenza, with a focus 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 2023 President's Budget request for RMS is $411.8 million, an increase of $13.2 million or 3.3 percent compared with the FY 2022 CR level. The budget increase will support ongoing administrative efforts and cover the FY 2023 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
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	$6,557,803,000	$6,342,756,000	$6,069,619,000
Rescission				$0
2023	$6,268,313,000			

[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	2022 Amount Authorized	FY 2022 CR	2023 Amount Authorized	FY 2023 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$6,069,619,000	Indefinite	$6,268,313,000
National Institute of Allergy and Infectious Diseases	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$6,069,619,000		$6,268,313,000

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Amounts Available for Obligation[1]

(Dollars in Thousands)

Source of Funding	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget
Appropriation	$6,069,619	$6,069,619	$6,268,313
Secretary's Transfer	-18,222	0	0
Subtotal, adjusted appropriation	$6,051,397	$6,069,619	$6,268,313
OAR HIV/AIDS Transfers	-2,548	0	0
Subtotal, adjusted budget authority	$6,048,849	$6,069,619	$6,268,313
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year (carryover)	0	0	0
Subtotal, adjusted budget authority	$6,048,849	$6,069,619	$6,268,313
Unobligated balance lapsing	-11	0	0
Total obligations	$6,048,838	$6,069,619	$6,268,313

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:
FY 2021 - $19,351 FY 2022 - $20,125 FY 2023 - $20,930

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Budget Authority by Object Class[1]

(Dollars in Thousands)

		FY 2022 CR	FY 2023 President's Budget	FY 2023 +/- FY 2022 CR
Total compensable workyears:				
	Full-time equivalent	2,180	2,180	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$204	$212	$9
	Average GM/GS grade	12.6	12.6	0.0
	Average GM/GS salary	$123	$128	$5
	Average salary, Commissioned Corps (42 U.S.C. 207)	$105	$110	$4
	Average salary of ungraded positions	$158	$162	$4
	OBJECT CLASSES	**FY 2022 CR**	**FY 2023 President's Budget**	**FY 2023 +/- FY 2022**
	Personnel Compensation			
11.1	Full-Time Permanent	196,859	205,702	8,844
11.3	Other Than Full-Time Permanent	82,689	87,028	4,339
11.5	Other Personnel Compensation	13,551	14,177	627
11.7	Military Personnel	3,541	3,713	173
11.8	Special Personnel Services Payments	26,409	27,844	1,435
11.9	**Subtotal Personnel Compensation**	**$323,048**	**$338,465**	**$15,417**
12.1	Civilian Personnel Benefits	107,609	112,353	4,744
12.2	Military Personnel Benefits	3,698	3,870	173
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$434,355**	**$454,688**	**$20,334**
21.0	Travel & Transportation of Persons	1,001	1,028	27
22.0	Transportation of Things	1,681	1,727	46
23.1	Rental Payments to GSA	47	48	1
23.2	Rental Payments to Others	0	0	0
23.3	Communications, Utilities & Misc. Charges	1,825	1,884	59
24.0	Printing & Reproduction	18	19	1
25.1	Consulting Services	202,167	206,714	4,547
25.2	Other Services	180,998	188,443	7,444
25.3	Purchase of Goods and Services from Government Accounts	592,744	606,799	14,055
25.4	Operation & Maintenance of Facilities	9,774	9,878	103
25.5	R&D Contracts	693,046	744,308	51,262
25.6	Medical Care	6,662	6,977	315
25.7	Operation & Maintenance of Equipment	32,905	33,871	965
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$1,718,297**	**$1,796,989**	**$78,692**
26.0	Supplies & Materials	62,696	64,408	1,712
31.0	Equipment	29,752	30,604	853
32.0	Land and Structures	2,438	2,492	54
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	3,817,505	3,914,422	96,917
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	3	3	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$5,635,264**	**$5,813,625**	**$178,360**
	Total Budget Authority by Object Class	**$6,069,619**	**$6,268,313**	**$198,694**

[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 2022 CR	FY 2023 President's Budget	FY 2023 +/- FY 2022
Personnel Compensation			
Full-Time Permanent (11.1)	$196,859	$205,702	$8,844
Other Than Full-Time Permanent (11.3)	82,689	87,028	4,339
Other Personnel Compensation (11.5)	13,551	14,177	627
Military Personnel (11.7)	3,541	3,713	173
Special Personnel Services Payments (11.8)	26,409	27,844	1,435
Subtotal Personnel Compensation (11.9)	**$323,048**	**$338,465**	**$15,417**
Civilian Personnel Benefits (12.1)	$107,609	$112,353	$4,744
Military Personnel Benefits (12.2)	3,698	3,870	173
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$434,355**	**$454,688**	**$20,334**
Travel & Transportation of Persons (21.0)	$1,001	$1,028	$27
Transportation of Things (22.0)	1,681	1,727	46
Rental Payments to Others (23.2)	0	0	0
Communications, Utilities & Misc. Charges (23.3)	1,825	1,884	59
Printing & Reproduction (24.0)	18	19	1
Other Contractual Services:			
Consultant Services (25.1)	202,167	206,714	4,547
Other Services (25.2)	180,998	188,443	7,444
Purchases from Government Accounts (25.3)	440,305	454,360	14,055
Operation & Maintenance of Facilities (25.4)	9,774	9,878	103
Operation & Maintenance of Equipment (25.7)	32,905	33,871	965
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$866,150**	**$893,265**	**$27,115**
Supplies & Materials (26.0)	$62,696	$64,408	$1,712
Subtotal Non-Pay Costs	**$933,372**	**$962,332**	**$28,959**
Total Administrative Costs	**$1,367,727**	**$1,417,020**	**$49,293**

NATIONAL INSTITUTES OF HEALTH
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Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2021 Final			FY 2022 CR			FY 2023 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Acquired Immunodeficiency									
Direct:	158	5	163	171	5	176	171	5	176
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	158	5	163	171	5	176	171	5	176
Division of Allergy, Immunology, and Transplantation									
Direct:	103	1	104	113	1	114	113	1	114
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	103	1	104	113	1	114	113	1	114
Division of Clinical Research									
Direct:	94	6	100	96	6	102	96	6	102
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	94	6	100	96	6	102	96	6	102
Division of Extramural Activities									
Direct:	236	-	236	260	-	260	260	-	260
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	236	-	236	260	-	260	260	-	260
Division of Intramural Research									
Direct:	734	11	745	749	11	760	749	11	760
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	734	11	745	749	11	760	749	11	760
Division of Microbiology and Infectious Diseases									
Direct:	181	8	189	193	8	201	193	8	201
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	181	8	189	193	8	201	193	8	201
Office of the Director									
Direct:	421	2	423	444	2	446	444	2	446
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	421	2	423	444	2	446	444	2	446
Vaccine Research Center									
Direct:	117	1	118	120	1	121	120	1	121
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	117	1	118	120	1	121	120	1	121
Total	2,044	34	2,078	2,146	34	2,180	2,146	34	2,180
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**								
2019	12.7								
2020	12.6								
2021	12.6								
2022	12.6								
2023	12.6								

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Detail of Positions[1]

GRADE	FY 2021 Final	FY 2022 CR	FY 2023 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	390,600	407,668	424,688
General Schedule			
GM/GS-15	210	215	215
GM/GS-14	433	448	448
GM/GS-13	414	431	431
GS-12	243	264	264
GS-11	117	126	126
GS-10	1	1	1
GS-9	77	79	79
GS-8	26	26	26
GS-7	51	52	52
GS-6	11	11	11
GS-5	4	4	4
GS-4	8	8	8
GS-3	6	6	6
GS-2	1	1	1
GS-1	3	3	3
Subtotal	1,605	1,675	1,675
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	9	9	9
Senior Grade	8	8	8
Full Grade	9	9	9
Senior Assistant Grade	4	4	4
Assistant Grade	0	0	0
Subtotal	30	30	30
Ungraded	509	509	509
Total permanent positions	1,619	1,620	1,620
Total positions, end of year	2,146	2,216	2,216
Total full-time equivalent (FTE) employment, end of year	2,078	2,180	2,180
Average ES salary	195,300	203,834	212,344
Average GM/GS grade	12.6	12.6	12.6
Average GM/GS salary	120,056	122,788	127,914

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