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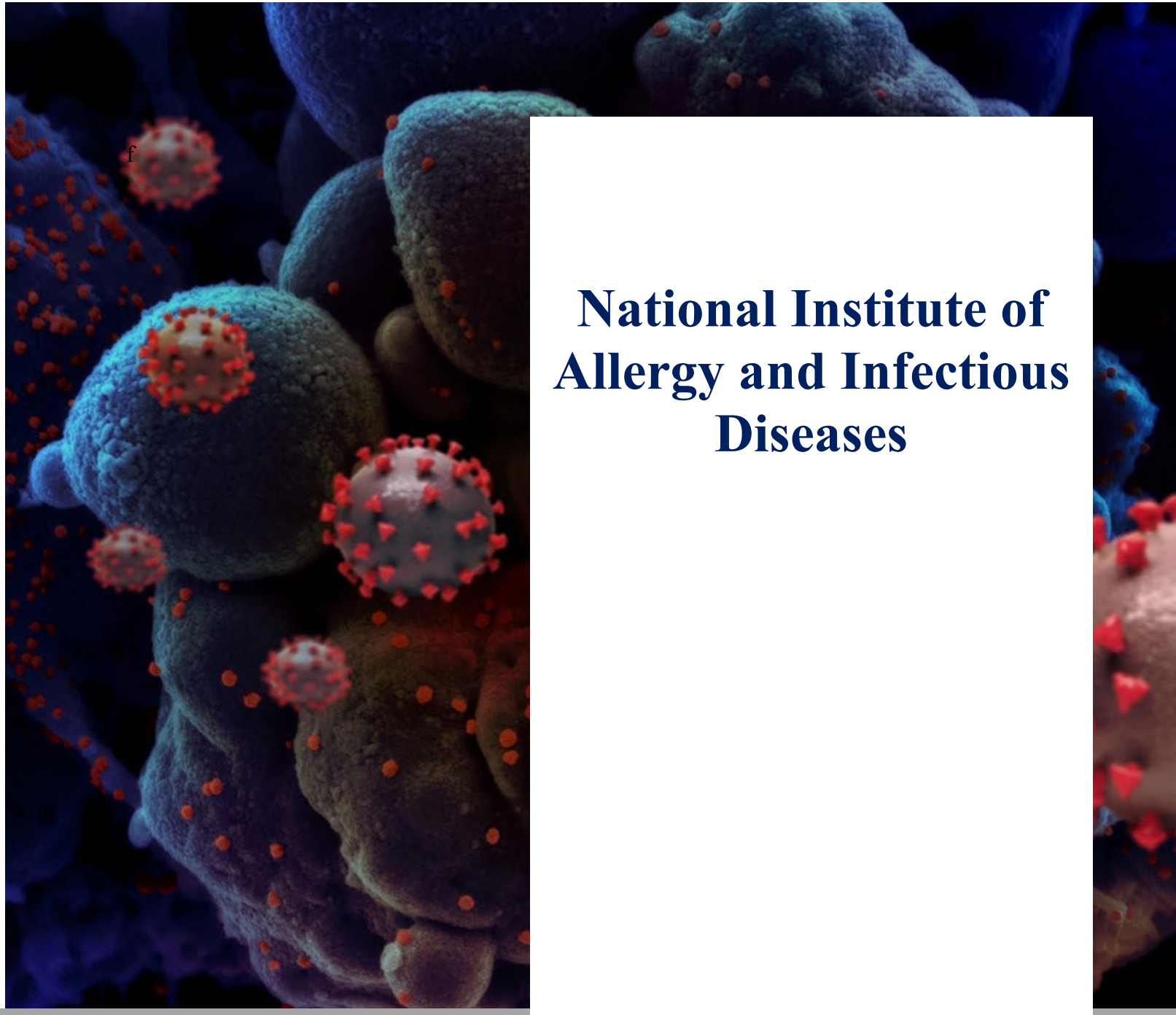

National Institute of Allergy and Infectious Diseases

CONGRESSIONAL JUSTIFICATION
FY 2024

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 2024 Budget Table of Contents

General Notes

1. FY 2023 Enacted levels cited in this document include the effects of the FY 2023 HIV/AIDS transfer, as shown in the Amounts Available for Obligation table.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

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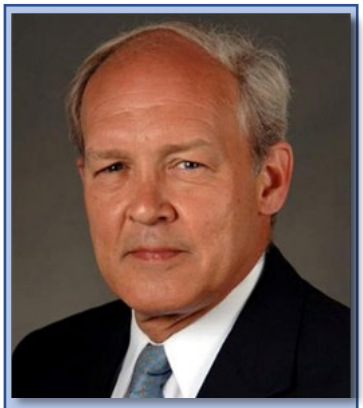
Director's Overview



NIAID Acting Director
Hugh Auchincloss, Jr., M.D.

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports biomedical research to develop and improve medical countermeasures to protect public health. As part of its dual mandate, NIAID also leads the research response to emerging disease threats that have a global impact. Together with other federal agencies, and with collaborators in industry, academia, and international research partners, NIAID continues to be at the forefront of biomedical science in addressing the research gaps in vaccine and therapeutic development for emerging infectious agents and diseases.

NIAID is dedicated to ensuring the translation of basic research advances into candidate vaccines and therapeutics to address public health needs for all. These efforts include the continued investment to maintain active partnerships and clinical infrastructure across the globe and facilitating diverse representation in clinical trials to ensure the medical countermeasures being developed will be safe and effective broadly. NIAID supports community engagement activities to increase the number of underrepresented minorities in clinical trials. For example, the HIV Vaccine Treatment Network (HVTN) established relationships with Black, African American, and Latinx communities to boost participation in trials of HIV interventions. These relationships proved critical during the COVID-19 pandemic when the HVTN rapidly enrolled participants from different ethnic groups across the country in clinical trials of COVID-19 vaccines. NIAID values the importance of a diverse workforce, both within the Institute and among the researchers that it supports, to advance its mission. With representatives across the Institute, the NIAID Diversity, Equity, Inclusion, and Accessibility (DEIA) Council is charged with fostering a diverse and inclusive workforce at NIAID and enhancing the diversity of the extramural workforce.

As the effects of the COVID-19 pandemic continue and as we monitor for emerging SARS-CoV-2 variants of concern, mitigating the impact of some existing medical countermeasures, advancing next-generation vaccines, diagnostics, and therapeutics is a priority. NIAID scientists and funded investigators are developing novel vaccine candidates with the goal of providing broad immunity against multiple coronavirus variants. One approach using mosaic nanoparticles displaying antigens derived from SARS-CoV-2 and other coronaviruses has demonstrated protection against multiple related viruses in animal models. Additionally, NIAID recently awarded several large program project grants to support a multidisciplinary approach to COVID-19 vaccines incorporating expertise in coronavirus biology, immunology, immunogen design, and innovative vaccine and adjuvant platform technologies. These resources will be applied to the development of vaccine candidates that provide broad immunity to multiple coronaviruses.

To increase the effectiveness of SARS-CoV-2 vaccines, researchers are advancing nasal vaccines that elicit rapid protection at the mucosal surfaces to prevent or limit infection and transmission. Recently, NIAID intramural investigators used modified vaccinia virus Ankara (MVA) as a vector to deliver the spike protein of SARS-CoV-2 intranasally in mice to generate a faster and

broader antibody response than traditional intramuscular vaccine administration methods. NIAID researchers also have developed a pediatric nasal vaccine that targets both SARS-CoV-2 and human parainfluenza virus type 3 (HPIV3), a common pediatric disease agent. This vaccine was safe and effective at preventing SARS-CoV-2 from spreading in the nose and lungs in animal models. Plans are currently underway to evaluate this vaccine candidate in a Phase 1 clinical trial in young children.

In addition to safe and effective vaccines, there remains a critical need to develop safe and effective antiviral drugs to prevent and treat COVID-19. NIAID, along with the National Center for Advancing Translational Sciences (NCATS), the NIH Office of Research Infrastructure Programs (ORIP), and the Administration for Strategic Preparedness and Response's Biomedical Advanced Research and Development Authority (BARDA), established the Antiviral Program for Pandemics (APP) to speed development of therapeutics for SARS-CoV-2 and other viruses with pandemic potential. As part of this effort, NIAID established nine Antiviral Drug Discovery (AViDD) Centers for Pathogens of Pandemic Concern. These centers will conduct research on early-stage identification and validation of novel viral targets that can inform the development of small molecule drugs and biotherapeutics.

The spread of mpox in the United States remains a concern as the need for vaccines for at-risk individuals has outpaced the available supply. Building on data from previous research studies, NIAID is evaluating the immunogenicity and safety of different administration routes of the currently approved JYNNEOS vaccine. Intradermal administration of this vaccine uses a lower dose to induce a similar immune response and can expand the number of available vaccine doses. This clinical trial is enrolling healthy volunteers and at-risk individuals, including those with controlled HIV infection, to ensure that any changes to the dosing strategy will be applicable to those who will benefit the most.

Currently, no approved treatments for human mpox disease are available, highlighting a gap in the need for interventions that may curb the current increase in cases of non-endemic and endemic mpox. Tecovirimat (TPOXX), approved by the U.S. Food and Drug Administration (FDA) for the treatment of human smallpox disease, has shown promise in animal models of mpox and in small numbers of human patients. NIAID is pursuing two separate clinical trials to evaluate the effectiveness of this drug in humans. Taking advantage of established infrastructure for the conduct of clinical trials for HIV interventions, the Study of Tecovirimat for Human mpox virus (STOMP) was launched in September 2022 in the United States to evaluate safety in an outpatient setting for both adults and children and determine if tecovirimat reduces the time to clinical resolution of disease. It is also critical to study drug efficacy in areas where the disease is endemic to ensure it is safe and effective in populations where the drug may be needed routinely. In this regard, NIAID has a longstanding and active collaboration with the National Institute for Biomedical Research (INRB) and the Ministry of Health in the Democratic Republic of the Congo (DRC). In October 2022, NIAID and IRNB launched a clinical trial in the DRC to detect whether adding tecovirimat to the standard of care will decrease time to disease resolution.

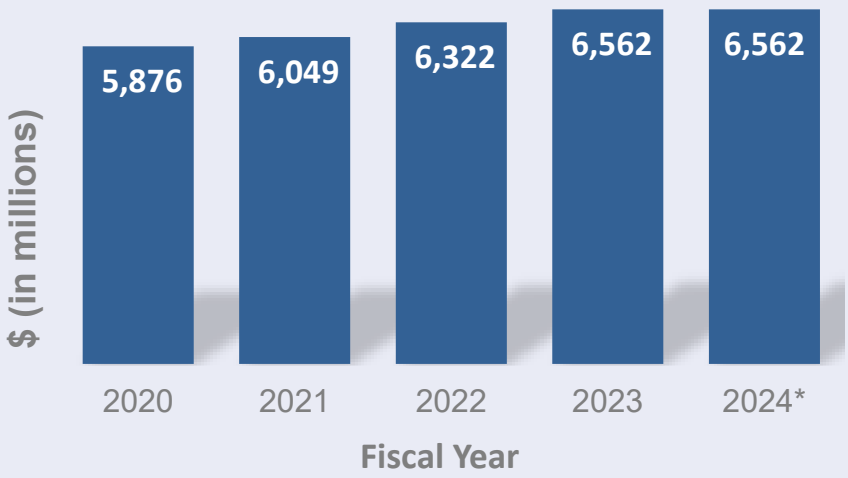
National Institute of Allergy and Infectious Diseases

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 60 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 Acting Director
Hugh Auchincloss, Jr., M.D.

FUNDING HISTORY



*President's budget request

FACTS AND FIGURES

2,017
FULL TIME EQUIVALENT EMPLOYEES

1,328
FUNDED PRINCIPAL INVESTIGATORS

Averaged over FY 2019-FY 2022

RESEARCH HIGHLIGHTS

It is important to understand the safety and immunogenicity of COVID-19 vaccine boosters of either the identical primary vaccine or one that is different. A study using the Moderna, J&J, and Pfizer vaccines as boosters showed that all had acceptable safety profiles and were immunogenic in adults who had completed a different primary vaccine series.

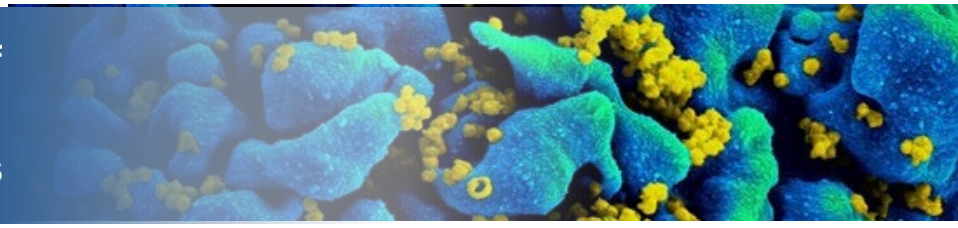
Malaria affects approximately 200 to 400 million people worldwide per year, making interventions to reduce morbidity and mortality a critical public health need. NIAID evaluated the safety and efficacy of two monoclonal antibodies, CIS43LS and L9LS, and demonstrated strong efficacy in experimental human challenge and field studies.

Preventing SARS-CoV-2 from establishing infection at the mucosal surfaces is the focus of next generation COVID-19 vaccines. NIAID supports the development of several nasal vaccine candidates that have shown promise in pre-clinical animal models. Efforts are underway to advance these into Phase 1 clinical trials.

Current typhoid vaccines are difficult to manufacture, making global implementation challenging. Addition of the Advax-CpG adjuvant, created within the NIAID Adjuvant Discovery Program, to the newly developed, low-cost Typhax vaccine elicited strong immune responses in animal studies. Early-stage clinical trials are planned in Australia.

Understanding the risk factors for COVID-19 disease is important for implementation of public health measures. The NIAID Human Epidemiology and Response to SARS-CoV-2 (HEROS) study found that people with food allergies are less likely to become infected with the virus. Asthma does not increase the risk of infection, but obesity and high body mass index do.

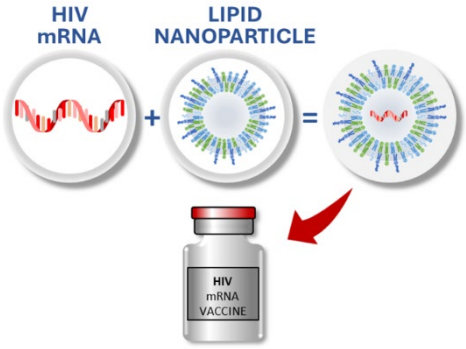
National Institute of Allergy and Infectious Diseases

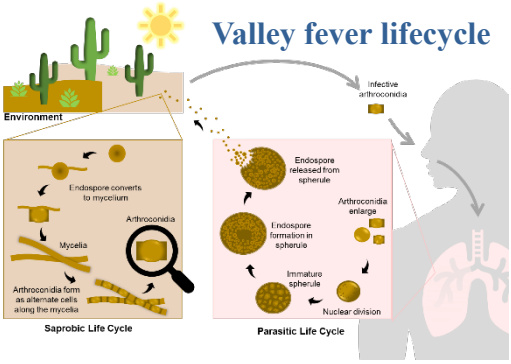


RESEARCH ADVANCES

The **mRNA platform technology** used to develop the successful COVID-19 vaccines is now being applied to develop several candidate vaccines against HIV.

- In 2021, NIAID scientists showed that an experimental HIV mRNA vaccine was safe and prompted the desired antibody and cellular immune responses in mice and non-human primates.
- In 2022, NIAID launched a clinical trial to examine whether three additional experimental HIV mRNA vaccines are safe and can induce immune responses in people. These investigational vaccine candidates are designed to induce immune responses against the surface HIV proteins that facilitate entry into human cells.



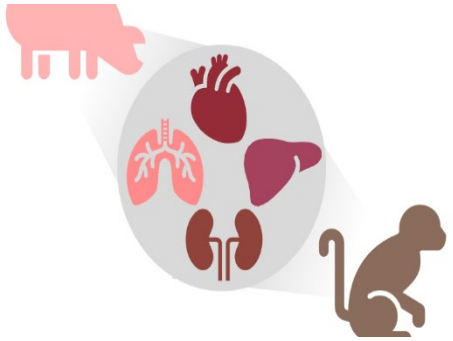


Valley fever, caused by the soil-dwelling fungi *Coccidioides immitis* and *Coccidiodes posadasii*, is endemic in parts of southwestern U.S. Infection with *Coccidioides* can cause fatigue, cough, fever, and rashes. Each year, thousands of people in the United States experience severe cases, which can lead to long-term respiratory symptoms.

- In 2022, NIAID awarded four grants to establish a network of Coccidioidomycosis Collaborative Research Centers to advance diagnostics, therapeutics, and vaccines for this fungal disease.
- In September 2022, NIAID published the Strategic Plan for Research to Develop a Valley fever Vaccine.

To address the shortage of **human organs for transplantation**, NIAID established The Immunobiology of Xenotransplantation Cooperative Research Program (IXCRP), which aims to develop preclinical porcine to non-human primate (NHP) models of islet, kidney, heart, lung, and liver xenotransplantation.

- NIAID investigators have overcome many obstacles to successful xenotransplantation with survival and function of pig kidney, and heart xenotransplants in NHPs extending up to 500 days and 6 months, respectively.
- These achievements are paving the way toward a xenotransplantation clinical trial.



Selected Future Research Initiatives

- **HIV CURE.** Projects focused on cure interventions administered during HIV infection near the start of antiretroviral therapy (ART) to achieve a sustained ART-free remission.
- **DURABLE PROTECTIVE IMMUNITY.** Research to improve understanding of how vaccines against infectious agents lead to durable protective immunity.
- **BACTERIAL VACCINES.** Research to develop vaccines against *E. coli*, *Salmonella*, and *Shigella,* which together cause a high burden of diarrheal disease globally.
- **DEIA.** Supporting new, early-stage, and at-risk investigators from diverse backgrounds, including groups underrepresented in the health sciences, to enhance the diversity of NIAID R01-funded investigators.

NIAID Commitment to DEIA

- Foster a workplace that embodies and values the perspectives of a diverse staff
- Fund an extramural research portfolio inclusive of the populations it serves
- Prioritize health equity in all research that NIAID conducts and supports

Major Changes in the Budget Request

Major changes by selected budget mechanism are briefly described below. The FY 2024 President's Budget request is $6,561.7 million, which is the same as the FY 2023 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) (-$7.5 million; total $3,842.4 million):
NIAID will support a total of 5,367 Research Project Grant (RPG) awards in FY 2024. The continued 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 decrease by $83.6 million or 10.5 percent in FY 2024, while noncompeting RPG funding will increase by $76.1 million or 2.7 percent. Overall RPG funding will decrease by 0.2 percent.

Research and Development Contracts (-$5.2 million; total $1,117.4 million):
NIAID will continue to support trans-NIH initiatives, including ongoing cybersecurity efforts, as well as other HHS-wide initiatives.

Intramural Research (+$8.5 million; total $861.5 million):
NIAID will continue 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 vector-borne diseases. The increased funding supports pay cost increases for intramural staff.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Budget Mechanism *

(Dollars in Thousands)

Mechanism	FY 2022 Final		FY 2023 Enacted		FY 2024 President's Budget		FY 2024 +/- FY 2023	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Research Projects:								
Noncompeting	3,671	$2,751,320	3,577	$2,864,434	3,749	$2,940,559	172	$76,126
Administrative Supplements	*(158)*	$59,493	*(92)*	$24,878	*(92)*	$24,878	*(0)*	$0
Competing:								
Renewal	145	$124,976	165	$148,567	161	$129,249	-4	-$19,318
New	1,085	$564,156	1,228	$651,206	1,210	$586,875	-18	-$64,331
Supplements	0	$0	0	$0	0	$0	0	$0
Subtotal, Competing	**1,230**	**$689,132**	**1,393**	**$799,774**	**1,371**	**$716,124**	**-22**	**-$83,649**
Subtotal, RPGs	4,901	$3,499,945	4,970	$3,689,086	5,120	$3,681,562	150	-$7,524
SBIR/STTR	251	$160,414	247	$160,819	247	$160,819	0	$0
Research Project Grants	5,152	$3,660,359	5,217	$3,849,905	5,367	$3,842,381	150	-$7,524
Research Centers								
Specialized/Comprehensive	34	$99,167	35	$101,713	35	$101,713	0	$0
Clinical Research	0	$0	0	$0	0	$0	0	$0
Biotechnology	0	$0	0	$0	0	$0	0	$0
Comparative Medicine	0	$770	0	$770	0	$770	0	$0
Research Centers in Minority Institutions	0	$0	0	$0	0	$0	0	$0
Research Centers	**34**	**$99,938**	**35**	**$102,483**	**35**	**$102,483**	**0**	**$0**
Other Research:								
Research Careers	327	$54,876	337	$57,291	337	$57,291	0	$0
Cancer Education	0	$0	0	$0	0	$0	0	$0
Cooperative Clinical Research	0	$0	0	$0	0	$0	0	$0
Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Minority Biomedical Research Support	0	$0	0	$232	0	$232	0	$0
Other	111	$78,677	115	$85,566	115	$85,566	0	$0
Other Research	**438**	**$133,553**	**452**	**$143,089**	**452**	**$143,089**	**0**	**$0**
Total Research Grants	5,624	$3,893,849	5,704	$4,095,477	5,854	$4,087,953	150	-$7,524
Ruth L Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	261	$12,225	264	$12,763	257	$12,763	-7	$0
Institutional Awards	954	$57,404	962	$59,930	942	$59,930	-20	$0
Total Research Training	**1,215**	**$69,629**	**1,226**	**$72,693**	**1,199**	**$72,693**	**-27**	**$0**
Research & Develop. Contracts	227	$1,134,291	122	$1,122,544	120	$1,117,358	-2	-$5,186
SBIR/STTR (non-add)	*(28)*	*($31,185)*	*(27)*	*($32,185)*	*(26)*	*($31,385)*	*-(1)*	*-($800)*
Intramural Research	954	$821,744	991	$852,970	991	$861,500	0	$8,530
Res. Management & Support	1,145	$402,667	1,189	$417,968	1,189	$422,148	0	$4,180
SBIR Admin. (non-add)		*($1,137)*		*($2,900)*		*($2,900)*		*($0)*
Construction		$0		$0		$0		$0
Buildings and Facilities		$0		$0		$0		$0
Total, NIAID	**2,099**	**$6,322,180**	**2,180**	**$6,561,652**	**2,180**	**$6,561,652**	**0**	**$0**

* 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, [$6,562,279,000]*$6,561,652,000.*

Summary of Changes

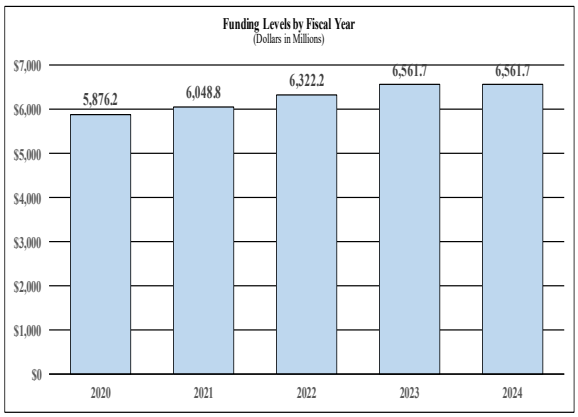
(Dollars in Thousands)

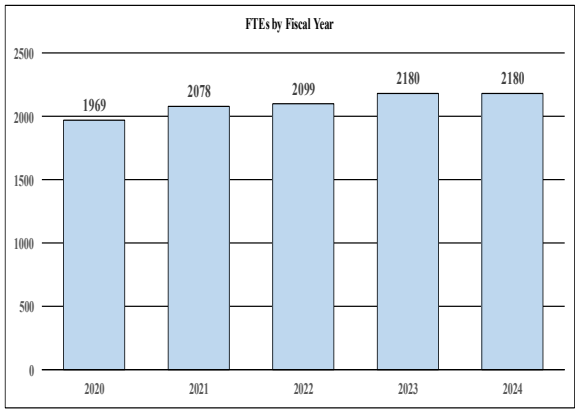
FY 2023 Enacted	$6,561,652
FY 2024 President's Budget	$6,561,652
Net change	$0

CHANGES	FY 2023 Enacted FTEs	FY 2023 Enacted Budget Authority	FY 2024 President's Budget FTEs	FY 2024 President's Budget Budget Authority	Built-In Change from FY 2023 Enacted FTEs	Built-In Change from FY 2023 Enacted Budget Authority
A. Built-in:						
1. Intramural Research:						
a. Annualization of FY 2023 pay and benefits increase		$224,157		$236,143		$2,488
b. FY 2024 pay and benefits increase		$224,157		$236,143		$8,592
c. Paid days adjustment		$224,157		$236,143		$863
d. Differences attributable to change in FTE		$224,157		$236,143		$0
e. Payment for centrally furnished services		$115,251		$117,095		$1,844
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		$513,562		$508,262		$12,141
Subtotal						$25,928
2. Research Management and Support:						
a. Annualization of FY 2023 pay and benefits increase		$232,881		$245,315		$2,577
b. FY 2024 pay and benefits increase		$232,881		$245,315		$8,915
c. Paid days adjustment		$232,881		$245,315		$897
d. Differences attributable to change in FTE		$232,881		$245,315		$0
e. Payment for centrally furnished services		$21,593		$21,938		$345
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		$163,494		$154,895		$3,703
Subtotal						$16,437
Subtotal, Built-in						$42,365

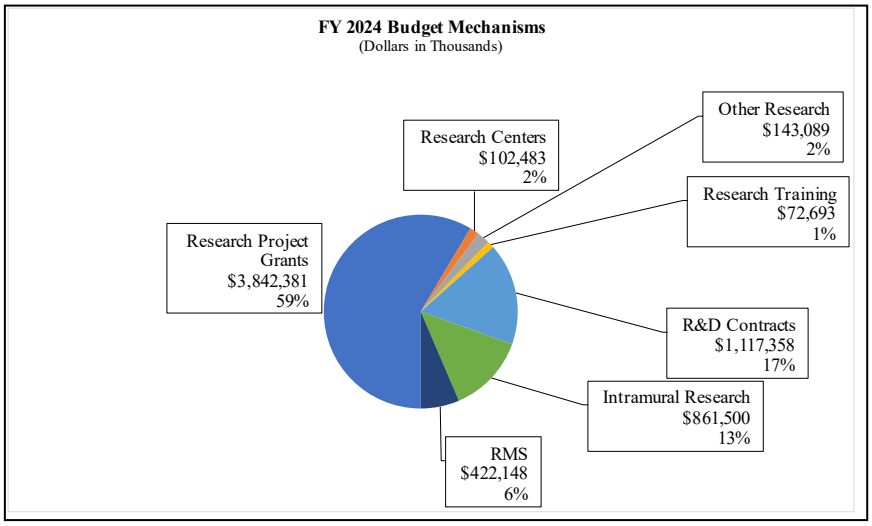
CHANGES	FY 2023 Enacted No.	FY 2023 Enacted Amount	FY 2024 President's Budget No.	FY 2024 President's Budget Amount	Program Change from FY 2023 Enacted No.	Program Change from FY 2023 Enacted Amount
B. Program:						
1. Research Project Grants:						
a. Noncompeting	3,577	$2,889,312	3,749	$2,965,438	172	$76,126
b. Competing	1,393	$799,774	1,371	$716,124	-22	-$83,649
c. SBIR/STTR	247	$160,819	247	$160,819	0	$0
Subtotal, RPGs	5,217	$3,849,905	5,367	$3,842,381	150	-$7,524
2. Research Centers	35	$102,483	35	$102,483	0	$0
3. Other Research	452	$143,089	452	$143,089	0	$0
4. Research Training	1,226	$72,693	1,199	$72,693	-27	$0
5. Research and development contracts	122	$1,122,544	120	$1,117,358	-2	-$5,186
Subtotal, Extramural		$5,290,714		$5,278,004		-$12,709
6. Intramural Research	991	$852,970	991	$861,500	0	-$17,398
7. Research Management and Support	1,189	$417,968	1,189	$422,148	0	-$12,257
8. Construction		$0		$0		$0
9. Buildings and Facilities		$0		$0		$0
Subtotal, Program	2,180	$6,561,652	2,180	$6,561,652	0	-$42,365
Total built-in and program changes						$0

History of Budget Authority and FTE:

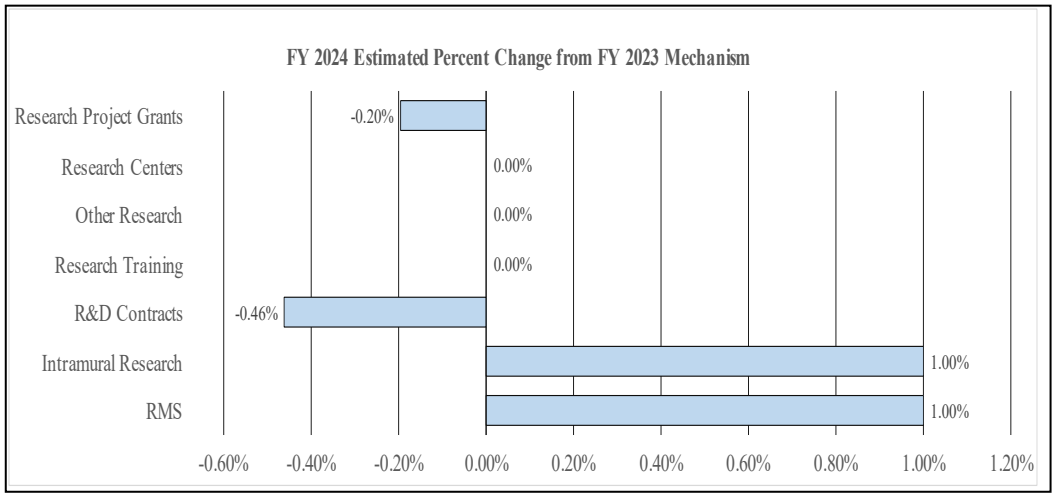




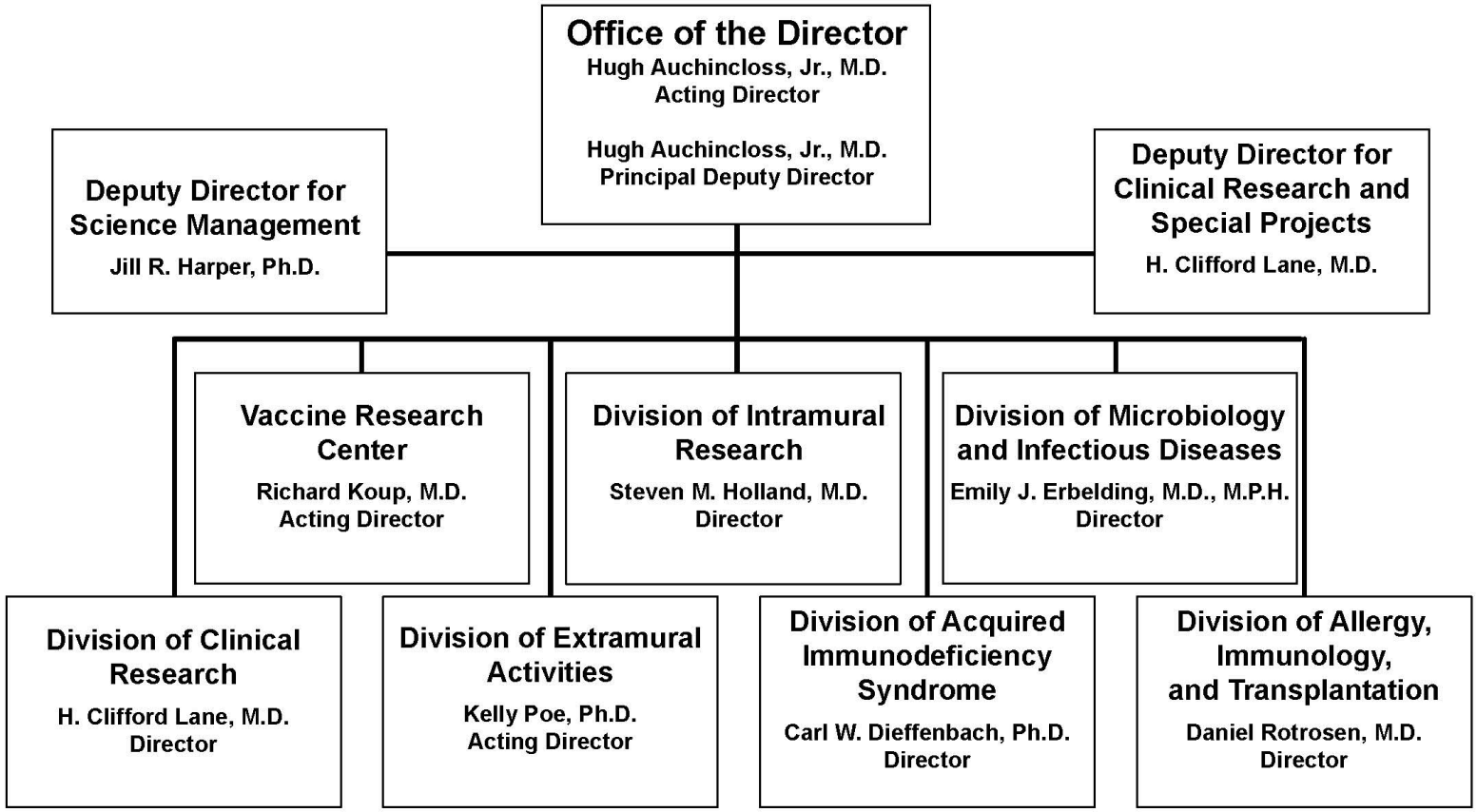
Distribution by Mechanism:



Change by Selected Mechanisms:



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



Budget Authority by Activity *
(Dollars in Thousands)

	FY 2022 Final		FY 2023 Enacted		FY 2024 President's Budget		FY 2024 +/- FY 2023 Enacted	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
HIV/AIDS [1]		$1,488,163		$1,535,408		$1,531,649		-$3,760
Biodefense & Emerging Infectious Diseases [2]		$2,147,097		$2,236,369		$2,231,341		-$5,028
Infectious & Immunological Diseases		$1,462,509		$1,518,937		$1,515,015		-$3,922
Subtotal, Extramural		**$5,097,769**		**$5,290,714**		**$5,278,004**		**-$12,709**
Intramural Research	**954**	**$821,744**	**991**	**$852,970**	**991**	**$861,500**	**0**	**$8,530**
Research Management & Support	**1,145**	**$402,667**	**1,189**	**$417,968**	**1,189**	**$422,148**	**0**	**$4,180**
TOTAL	**2,099**	**$6,322,180**	**2,180**	**$6,561,652**	**2,180**	**$6,561,652**	**0**	**$0**

* Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

[1] Reflects NIAID extramural total for HIV/AIDS. NIAID-wide totals are (in thousands) $1,779,113 in FY 2022; $1,788,843 in FY 2023; and $1,798,843 in FY 2024.

[2] Reflects NIAID extramural total for Biodefense. NIAID-wide totals are (in thousands) $2,371,416 in FY 2022; $2,495,748 in FY 2023; and $2,594,251 in FY 2024.

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 2022 Final	FY 2023 Enacted	FY 2024 President's Budget	FY 2024 +/- FY 2023
BA	$6,322,180,000	$6,561,652,000	$6,561,652,000	0
FTE	2,099	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 2024 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 FY 2024 President's Budget request is $6,561.7 million, which is equal to the FY 2023 enacted 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.

The Institute remains focused on high priority areas of research such as other emerging infectious diseases, agents with bioterrorism potential, HIV/AIDS, Mpox, influenza, tuberculosis, malaria, drug-resistant microbes, vector-borne diseases, autoimmune disorders, asthma, and allergies and continues to fund research to understand and develop medical countermeasures to address the COVID-19 pandemic. In FY 2024, 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. Additionally, NIAID will continue efforts to develop 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.

Program Descriptions

HIV/AIDS

Decades of basic and clinical research sponsored by NIAID have revolutionized the medical treatment of people with HIV/AIDS. Optimization of antiretroviral drug regimens and the establishment of treatment paradigms, including stressing early treatment and adherence, have transformed HIV infection from an almost uniformly fatal infection into a manageable chronic condition. Capitalizing on progress in the treatment of HIV/AIDS, the HHS initiative "Ending the HIV Epidemic in the United States" (EHE) aims to reduce new HIV infections in the United States by 90 percent by 2030. To support this goal, NIAID supports research that pairs researchers with community partners to pursue creative, locally defined, and culturally sensitive concepts relevant to their region to diagnose, treat, prevent, and respond to HIV infection. Additionally, the Centers for AIDS Research (CFARs) are investigating how to best deliver evidence-based interventions and services in regions of the country with the highest rates of HIV, focusing on individuals with a disproportionate risk of HIV infection, such as Black and Latinx populations.

Unlike current antiretroviral treatment (ART) regimens that require daily dosing, long-acting antiretrovirals would revolutionize the control and prevention of HIV. A recent NIAID Phase 1 study demonstrated that a therapeutic approach using two broadly neutralizing antibodies (bNAbs) against HIV was effective in suppressing HIV viral loads for extended periods of time in the absence of ART. Unfortunately, this treatment was not effective for participants infected with a form of HIV that is resistant to either bNAb. Results of this research are paving the way for new alternatives to daily ART for people living with HIV. For example, NIAID scientists and their collaborators isolated a naturally occurring bNAb, dubbed VRC07, and developed a drug-delivery system that uses adeno-associated virus serotype 8 (AAV8) to deliver the gene encoding this bNAb to a person with HIV, giving the patient the ability to produce their own anti-HIV therapeutic. A Phase 1 clinical trial of AAV8-VRC07 showed that it was safe when administered intramuscularly, and participants produced sustained levels of VRC07. Efforts to characterize the factors that determine how much bNAb is produced by human cells are underway as participants in this study continue to be monitored.

Curing HIV, a major NIAID priority, will require eradicating or otherwise controlling the HIV reservoir – pockets of virus that lie dormant in cells in the body until they are activated when ART is interrupted. NIAID is evaluating several bNAbs for HIV eradication, to be used either by themselves or in combination with compounds that reactivate latent, or non-replicating, HIV, allowing ART and the body's immune system to attack the virus. An observational study, conducted through the International Maternal Pediatric Adolescent AIDS Clinical Trial (IMPAACT) network, is following people living with HIV who undergo stem cell transplants because of a cancer diagnosis. Prior to transplant, scientists genetically remove the CCR5 co-receptor from the patient's stem cells, which HIV uses to infect cells, ultimately preventing descendants of those stem cells from expressing CCR5. In one study, an individual with HIV who stopped ART 37 months after receiving a transplant has no detectable HIV 14 months later. This example, taken together with similar data from two previously reported cases from other countries, provides evidence that although not a universal cure, CCR5-deleted stem cell

transplantation should be considered to achieve HIV remission and cure for people living with HIV who require such a transplant for other diseases.

While rates of mother-to-child transmission of HIV have fallen in the last decade, research is ongoing to optimize prevention of HIV transmission from mother to child and to evaluate the factors that impact ART efficacy during pregnancy. Recent studies indicate that pregnancy may affect the way antiretroviral drugs are metabolized, rendering ART less effective. In one NIAID-supported study, the combination of two antiretroviral drugs – darunavir and cobicistat – was tested in pregnant women with HIV in the United States. Researchers found that levels of both drugs were much lower during the second and third trimesters when compared with postpartum levels, suggesting that standard dosing of ART during pregnancy may increase the risk of treatment failure and mother-to-child transmission. In addition, a recent Phase 3 clinical trial was conducted across nine countries to examine the safety and efficacy of three different ART regimens in pregnant women. The study showed that when started during pregnancy, dolutegravir-containing regimens were superior at suppressing viral levels compared with other regimens. The study also identified ART regimens that resulted in the lowest frequency of adverse pregnancy outcomes and neonatal deaths. NIAID research continues to pave the way for the development of optimized strategies to prevent perinatal HIV transmission in the United States and around the world.

mRNA VACCINES FOR HIV

Building on the discoveries that enabled the remarkable success of COVID-19 mRNA vaccines, researchers are applying mRNA platform technology to develop candidate HIV vaccines. For example, one vaccine candidate evaluated in mice and nonhuman primates (NHPs) provides instructions for making two key HIV proteins, envelope (Env) and Gag. The study showed that the Env protein produced by the experimental HIV vaccine closely resembled the Env protein of the whole HIV virus, mimicking natural infection, and likely playing a role in generating the desired immune response to protect against HIV. Furthermore, this candidate vaccine was well-tolerated and prompted the desired antibody and cellular immune responses. Studies are underway to optimize the vaccine to increase its efficacy and reduce the number of booster vaccinations required to produce a robust immune response.

After nearly four decades of effort by a global research community, an effective vaccine to prevent HIV remains an elusive goal. The application of mRNA platform technology towards this goal represents a promising path forward. NIAID recently launched a Phase 1 clinical trial to examine whether three experimental HIV mRNA vaccines are safe and can induce an immune response in people (the HVTN 302 study). Each investigational vaccine candidate is designed to present the surface HIV proteins that facilitate entry into human cells. This study, which will enroll adults at 11 U.S. sites, is expected to be completed in July 2023.

Along with advancing HIV prevention strategies, such as microbicides, the development of a safe and effective HIV vaccine remains key to realizing an end to the HIV epidemic. One approach to vaccine development is identifying novel HIV vaccine immunogens, or proteins that induce a protective immune response. NIAID scientists developed a vaccine candidate, called Trimer 4571, composed of a stabilized HIV-1 envelope protein trimer. A Phase 1 clinical trial of Trimer 4571 with alum (a common vaccine adjuvant) showed that it was safe and well-tolerated, but it produced low levels of neutralizing antibodies. Animal model studies suggest that the addition of a priming molecule may overcome this and clinical trials to validate this finding are in development. NIAID continues to investigate additional strategies for

developing an HIV vaccine, including mRNA vaccines (see HIV program portrait) with multiple candidates in various stages of development.

Budget Policy:
The FY 2024 President's Budget request for the extramural component of NIAID HIV/AIDS research is $1,531.6 million, which is a reduction of $3.8 million or 0.2 percent from the FY 2023 enacted 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 2024 request includes $26.0 million, unchanged from the FY 2023 enacted level, to support ongoing research under the Ending the HIV Epidemic in the U.S. (EHE) initiative. NIAID will continue to support the Centers for AIDS Research (CFAR) activities and related efforts, which offer evidence-based practices on prevention and treatment to initiative partners and support for evaluating the initiative.

Biodefense and Emerging Infectious Diseases
The emergence and re-emergence of infectious diseases, accelerated in part by factors such as human encroachment into, and modification of, wildlife habitats, climate change, and declines in biodiversity, threatens the health of people worldwide. As part of its dual mandate, NIAID continues to conduct and support research to better understand viruses, bacteria, and other infectious agents of public health concern. This has been underscored during the COVID-19 pandemic. NIAID continues to lead the U.S. government biomedical research response in developing safe and effective COVID-19 countermeasures, including assessing booster vaccine strategies for healthy adults and those with compromised immune systems.

For example, the COVID-19 Variant Immunologic Landscape (COVAIL) trial is aiming to understand whether different vaccine regimens, including vaccines targeting SARS-CoV-2 variants, can broaden immune responses in adults who already have received their primary series plus one booster shot. Additionally, the NIAID Infectious Diseases Clinical Research Consortium conducted a "mix and match" clinical trial in which investigators administered COVID-19 booster vaccines to adults in the United States who had previously received a primary COVID-19 vaccination series from one manufacturer. Some participants received the same brand of vaccine as their primary series, and others received a vaccine from a different manufacturer. Results showed that for all combinations of primary and booster vaccines, immune responses over time resulted in increased neutralizing antibody levels in the recipients. For some individuals with suppressed or compromised immune systems, the standard vaccine dosing regimen may not be sufficient to elicit a protective immune response. To address this issue, NIAID is sponsoring two Phase 2 trials: the first is assessing the immune response to a booster dose of a COVID-19 mRNA vaccine in kidney and liver transplant recipients, either alone or with a transient reduction in immunosuppressive medication; and the second is assessing the immune response to booster doses of COVID-19 vaccines in people with autoimmune diseases, with or without a brief cessation of the immunosuppressive drugs.

Pediatric populations have been hit hard by the COVID-19 pandemic – both with acute infections and with longer lasting impacts such as multisystem inflammatory syndrome in

children (MIS-C) and post-acute sequelae of SARS-CoV-2 (PASC; also known as Long COVID). Several ongoing NIAID studies are focused on understanding the outcomes and long-term impacts of this virus on children's health. The Pediatric Research Immune Network on SARS-CoV-2 and MIS-C (PRISM) study enrolled 244 children and young adults ages 20 years or younger from diverse racial and ethnic backgrounds at approximately 20 sites nationwide to observe short- and long-term outcomes of children infected with SARS-CoV-2 and characterize the immunologic pathways leading to those outcomes. Another study, which is part of NIH's Researching COVID to Enhance Recovery (RECOVER) Initiative, will track up to 1,000 children and young adults who previously tested positive for COVID-19 to evaluate the impact of COVID-19 on their physical and mental health over three years. Results from a recently completed study evaluating immune responses in children with SARS-CoV-2 or MIS-C indicate that children's immune systems respond differently to the two conditions, assisting physicians in properly treating children with MIS-C.

The devastation of the COVID-19 pandemic affirmed the impact that outbreaks of emerging and re-emerging infectious disease can have on human health globally. As such, NIAID has taken great strides to prepare for future outbreaks by developing its Pandemic Preparedness Plan.[1] The Plan aligns with both the American Pandemic Preparedness Plan: Transforming our Capabilities and the National Biodefense Strategy and Implementation Plan on the development of vaccines, therapeutics, and diagnostics for pathogens that could cause significant disease and lead to a future pandemic. The Plan's goals are to characterize pathogens of concern, shorten timelines between pathogen emergence and authorization/approval of medical countermeasures (MCMs), and eliminate gaps in research, infrastructure, and technology. Within the Plan, biomedical research is prioritized on prototype pathogens, representative viruses from 10 families of pandemic potential. The in-depth characterization of these prototype pathogens offers a viable pathway to gain knowledge and develop MCMs that may be applicable to other viruses in the same family. NIAID hosted a workshop that brought together experts in virology to discuss prioritizing prototype pathogens within these families for MCM development. NIAID will continue to invest in the Pandemic Preparedness Plan to expand these activities to their full potential.

[1] https://www.niaid.nih.gov/sites/default/files/pandemic-preparedness-plan.pdf

NIAID also has a commitment to advance research on vector-borne diseases, including those transmitted by mosquitos and ticks. For example, NIAID scientists designed a virus-like particle (VLP) vaccine candidate (abbreviated WEVEE) that expresses proteins from the outer shells of three related alphaviruses, western equine encephalitis virus (WEEV), eastern equine encephalitis virus (EEEV), and Venezuelan equine encephalitis virus (VEEV) to prompt a protective immune response. WEEV, EEEV, and VEEV are spread to humans through the bites of infected mosquitoes and can lead to flu-like symptoms and in some cases to severe neurological damage or death. A Phase 1 study testing WEVEE vaccine showed that it was safe, well-tolerated, and induced an antibody response. NIAID also has developed a promising VLP vaccine for the mosquito-borne Chikungunya virus, which generates an immune response lasting at least 16 months. Lyme disease, transmitted by blacklegged ticks, accounted for 82 percent of all tick-borne disease cases in the United States from 2004 to 2016. Current antibiotics to treat Lyme disease are broadly acting and disrupt the patient's microbiome. NIAID-funded researchers have discovered a specific antibiotic that in mice can selectively clear *Borrelia burgdorferi*, the bacterium that causes Lyme disease. This finding holds potential as an alternative therapeutic option. NIAID also is investigating therapies for people with Lyme disease who do not respond well to initial treatment and continue to suffer symptoms.

Food- and water-borne bacterial pathogens, including *Escherichia coli*, *Salmonella enterica serotype* Paratyphi A*, Shigella flexneri,* and *Shigella sonnei*, significantly impact public health and often lead to lifelong consequences that negatively impact physical health and cognitive development, especially for infants and children. In FY 2023, NIAID will award research grants for projects to advance development of vaccine candidates against these bacteria. NIAID's Antibacterial Resistance Leadership Group (ARLG), a global consortium that leads a comprehensive clinical research agenda, is also

VACCINE RESEARCH TO COMBAT VALLEY FEVER

Valley fever, a disease caused by the soil-dwelling fungi *Coccidioides immitis* and *Coccidioides posadasii*, is endemic in parts of the southwestern United States, as well as in Mexico and Central and South America. Infection with Coccidioides is often asymptomatic in people, but some suffer from fatigue, cough, shortness of breath, fever, and rashes. Each year, thousands of people in the United States experience severe *Coccidioides* infections, which can lead to long-term respiratory symptoms. In rare instances, the infection can spread outside of the lungs and cause meningitis, skin lesions, and even death.

In February 2022, NIAID established a network of Coccidioidomycosis Collaborative Research Centers to advance diagnostics, therapeutics, and vaccines for this fungal disease. Scientists supported within this network will work collaboratively by pooling resources and expertise. To accelerate progress where obstacles and significant gaps in scientific knowledge exist for Valley fever research, NIAID published the Strategic Plan for Research to Develop a Valley Fever Vaccine in September 2022. This plan is organized around three interdependent strategic priorities to advance research on a Valley fever vaccine: 1) understanding Coccidioides pathogenesis and host responses, 2) developing tools and resources to support Coccidioides vaccine research, and 3) advancing strategies to prevent Valley fever. Ongoing NIAID research aims to characterize disseminated coccidioidomycosis (DCM), when the fungus infects other body parts, and refractory coccidioidomycosis (RCM), when the fungus stays in the lungs for longer than six months. NIAID researchers are examining multiple immune factors, characterizing the demographics of patients afflicted with DCM and RCM, and examining the genetic similarities of the infecting organisms. This information will reveal pathways that might be targets for therapeutic intervention and vaccine development.

prioritizing the development of better countermeasures against antibiotic-resistant bacteria. ARLG researchers initiated a Phase 2b trial to test the antibiotic dalbavancin for safety and efficacy in treating complicated *Staphylococcus aureus* blood infections. This trial will ascertain whether dalbavancin is better than standard antibiotics for the treatment of complicated *S. aureus* bacteremia.

Most bacteria, viruses, and other microbes multiply rapidly and can evolve and develop resistance to antimicrobial drugs, making them increasingly difficult -- and sometimes impossible -- to treat. Accurately diagnosing the type of pathogen causing infection is one step in curbing the threat of antimicrobial resistance. In FY 2023, NIAID will support research projects that focus on developing diagnostics that can rapidly and accurately identify the culprit microbe and provide clinicians with information for the most effective treatment. NIAID also is supporting research using bacteriophages, or phages, to treat antibiotic-resistant infections. Phages are viruses that can directly infect and destroy bacteria, bypassing bacterial antibiotic resistance mechanisms. ARLG scientists are conducting a clinical trial assessing the safety and microbiological activity of a single dose of a bacteriophage cocktail to treat *Pseudomonas aeruginosa* infections in cystic fibrosis patients. Additionally, a NIAID-funded clinical trial will evaluate the clinical safety and efficacy of ShigActive, a bacteriophage cocktail, to treat *Shigella* infections. *Shigella* bacteria are the causative agents for shigellosis and dysentery.

Tuberculosis (TB) is the second leading cause of death after SARS-CoV-2 among infectious diseases globally.[2] Additional research is needed to discover and improve diagnostics, therapeutics, and vaccines to alleviate the global burden of TB. In FY 2024, NIAID will establish a consortium of TB preclinical and clinical experts to systematically refine preclinical models with clinical data and identify the most efficacious drug combination regimens for future clinical trials. A notable advance in TB prevention supported by NIAID is a three-month course of weekly isoniazid and rifapentine, referred to as 3HP. The IMPAACT network recently conducted a clinical study that found 3HP is well-tolerated and safe in pregnant women with latent TB who are also living with HIV. These promising results pave the way for larger studies to address maternal safety, increase diversity in study participants, and understand the influence of ART on the TB drug levels in pregnant women living with HIV. NIAID-funded researchers also are advancing novel TB vaccination strategies, including a spray-dried TB vaccine that was effective in controlling TB in mice. Spray-dried vaccines could be more easily shipped globally and have dosage and administration route flexibility.

Each year, seasonal influenza sickens millions and causes thousands of hospitalizations and flu-related deaths.[3] In the hopes of eliminating the need for annual vaccination, universal or broadly protective flu vaccines are being developed to generate long-lasting immune responses against many existing or emerging influenza strains. For example, a Phase 1 clinical trial, now completely enrolled, is testing the safety of a novel influenza candidate vaccine, BPL-1357, and its ability to prompt immune responses. BPL-1357 is a whole-virus vaccine made up of four strains of non-infectious, chemically inactivated, low-pathogenicity avian flu virus. NIAID researchers also are utilizing a ferritin-based and computationally designed self-assembling nanoparticle vaccine platform to make next-generation vaccines against influenza. Advantages

[2] www.who.int/news-room/fact-sheets/detail/tuberculosis
[3] www.cdc.gov/flu/about/burden/index.html

of these approaches include the ability to target the unchanging stem region of the influenza virus, eliminating the need to reformulate a seasonal vaccine each year, and the fact that they do not require growing live influenza virus like traditional vaccines. The results of the clinical trial of a ferritin nanoparticle-based vaccine showed that neutralizing antibodies were detected in all participants that were durable up to six months after the second injection, indicating that this is a potential strategy for universal influenza vaccine development. NIAID is also assessing alternate administration routes, including a recent candidate vaccine administered intranasally together with an immune-boosting adjuvant.

Budget Policy:
The FY 2024 President's Budget request for the extramural component of Biodefense and Emerging Infectious Diseases research supported by NIAID is $2,231.3 million, which is $5.0 million or 0.2 percent lower than the FY 2023 enacted level. NIAID will continue to conduct and support research to better understand, prevent, and treat infectious diseases of public health concern.

The FY 2024 request will support the development of medical countermeasures and new platform technologies as part of a strategy to address emerging and re-emerging infectious disease pathogens. The budget includes $270.0 million, equal to the FY 2023 enacted level, to sustain 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.

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. Such diseases include malaria, neglected tropical diseases, hepatitis, sexually transmitted infections (STIs, including herpes simplex virus), 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, and advancing research on hepatitis B and C viruses are only a few examples of how NIAID will begin to address the magnitude of disease burden imposed by infectious and immune-mediated diseases.

The prevalence of food allergy among children under 18 has been increasing, and today peanut allergy affects about 2 percent of children in the United States, or nearly 1.5 million individuals. NIAID's Immune Tolerance Network completed a clinical trial, called IMPACT, that investigated whether giving gradually increasing doses of peanut protein could lead to allergy remission in young children with severe peanut allergy. The clinical trial found that peanut protein, given orally, safely desensitized most children and led to remission of peanut allergy in one-fifth of the participants. The results also pointed to a window of opportunity in early childhood when oral immunotherapy may be successful. NIAID also is advancing similar tolerization strategies for those suffering from other allergies. In another approach, the CATNIP study tested cat immunotherapy together with a monoclonal antibody against TSLP, an immune factor that plays an important role in allergy. The results demonstrated that adding antibody

improved the response while on immunotherapy and extended the response after immunotherapy was stopped. This study supports the concept that allergen-specific immunotherapy can be enhanced by combination with other immune-modulating agents.

Asthma is a chronic lung disease that reduces the quality of life, is a major reason for school absenteeism, and causes life-threatening attacks leading to numerous emergency department visits and hospitalizations. In the United States, severe asthma disproportionately affects Black and Hispanic children in low-income urban environments. To address this disparity, a NIAID-supported study recently found that a monoclonal antibody, mepolizumab, decreased asthma attacks by 27 percent in Black and Hispanic children and adolescents who are prone to asthma attacks and live in low-income urban neighborhoods. NIAID also launched the Prevention of Asthma Exacerbations Using Dupilumab in Urban Children and Adolescents (PANDA) trial to examine if dupilumab, another monoclonal antibody, can reduce asthma attacks and improve lung function and asthma symptoms in children with poorly controlled allergic asthma.

Malaria, a mosquito-borne disease caused by *Plasmodium* parasites, remains a major global public health problem and a priority area of NIAID research. NIAID continues to support basic and clinical research to accelerate malaria vaccine discovery. In pregnant women, malaria-infected red blood cells collect in vascular spaces of the placenta. This can result in inflammatory immune responses leading to various adverse pregnancy outcomes, including severe maternal anemia, fetal growth restriction, premature delivery, and maternal and/or perinatal mortality. NIAID scientists identified a protein highly expressed on the surface of *Plasmodium* parasites called PfCSA-L that is a potential target for vaccine development. A new and promising approach to prevent malaria is administering a monoclonal antibody against the sporozoite, the infectious form of the parasite. NIAID conducted a Phase 1 clinical trial to evaluate a single injection of a candidate monoclonal antibody known as L9LS, developed by scientists at the NIAID Vaccine Research Center (VRC). L9LS was found to be safe and highly protective in U.S. adults following controlled human challenge with malaria. It is now being evaluated for malaria prevention in infants and children in Mali and Kenya, where the disease is endemic. L9LS is highly potent, allowing for subcutaneous injection, a more cost-effective and feasible route of administration than intravenous injection and could potentially be

XENOTRANSPLANTATION RESEARCH TO ADDRESS ORGAN DONATION SHORTAGES

Since 2016, approximately 28,000 new people have been added to the heart transplant wait-list and 1,687 have died while waiting. To address transplant needs and shortages of human organs, NIAID established The Immunobiology of Xenotransplantation Cooperative Research Program (IXCRP). Xenotransplantation is a transplant from one species to another. The goal of this program is to develop preclinical pig to NHP models of islet, kidney, heart, lung, or liver transplantation. Genetically modified (GM) pigs offer unique benefits as xenograft donors because they are anatomically and physiologically similar to humans. These GM pigs are developed through an iterative process of gene editing to ensure each gene modification dampens the recipient immune response to the transplanted organ, thus increasing xenograft survival.

Research supported by the IXCRP laid the foundation for the first pig-to-human heart transplant that took place in 2022. Following the surgery, the 57-year-old male recipient had excellent cardiac function. This initial success has encouraged expansion of both preclinical and clinical research activities. NIAID has supported xenotransplantation research since 2003 and will continue to ensure high scientific, regulatory, and ethical standards in this rapidly evolving field.

used as a single dose to prevent malaria in infants, young children, and pregnant individuals. In a study focused on the mosquito vector, an engineered symbiotic bacterium protected mosquitos from *Plasmodium falciparum* infection by secreting a substance that selectively kills *Plasmodium* parasites. This bacterium disseminates through mosquito populations, rendering them resistant to malaria infection and providing a potential tool for blocking malaria transmission to humans if disseminated in the field.

Sexually transmitted infections (STIs) are an important global health priority because of their potentially devastating impact on long-term health. When left untreated, STIs can cause long-term health problems, including infertility and neurological impairment, making prevention a critical public health need. NIAID conducted a clinical trial to evaluate the use of doxycycline post-exposure prophylaxis (or DoxyPEP). DoxyPEP is a targeted intervention in which an antibiotic is given to high-risk individuals within three days of having sex without a condom as a method to prevent STIs. During a planned safety oversight meeting, it was recommended that everyone in the control arm be offered active therapy because the treatment effectively reduced the number of gonorrhea, chlamydia, and syphilis infections in men who have sex with men and transgender women who are living with HIV or are taking HIV pre-exposure prophylaxis (PrEP). While this study indicates DoxyPEP may be an effective strategy to prevent STIs in high-risk individuals, further investigation into the impact of this treatment on the development of antimicrobial resistance is warranted.

Hepatitis C is one of the most common bloodborne infections in the United States, and infections are on the rise among young adults. NIAID researchers and their collaborators recently characterized the interactions of a hepatitis C virus (HCV) protein with a host cell protein that facilitates viral entry into the host cell. The results of this work may provide the foundation for an HCV vaccine. Hepatitis B virus (HBV) infection may cause short-term illness; however some individuals may develop a chronic infection, particularly those infected early in life. Chronic infection may lead to serious complications, such as cirrhosis, liver cancer, and liver failure. Left untreated, these complications can be life-threatening. While there is no cure for hepatitis B, highly effective vaccines can prevent HBV infection, and oral antiviral agents and other therapeutics can slow the progression of hepatitis B complications. NIAID recently led the trans-NIH effort to update the Strategic Plan for NIH Research to Cure Hepatitis B[4], a roadmap for ending the hepatitis B epidemic, to incorporate lessons learned from the COVID-19 pandemic and recent advances in technology. The plan aligns with the HHS Viral Hepatitis National Strategic Plan[5] and is designed to be a part of NIH's ongoing response to the effects of this disease.

Budget Policy:
The FY 2024 President's Budget request for the extramural component of Infectious and Immunologic Diseases research is $1,515.0 million, which is a reduction of $3.9 million or 0.3 percent compared with the FY 2023 enacted level. NIAID will continue to advance long-range research priorities in infectious and immunologic diseases. The FY 2024 request will support NIAID's commitment and long-term interest in fundamental immunology, as well as research on

[4] https://www.niaid.nih.gov/sites/default/files/Trans-NIH-Hep-B-Strategic-Plan-2019.pdf
[5] https://www.hhs.gov/sites/default/files/Viral-Hepatitis-National-Strategic-Plan-2021-2025.pdf

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

Intramural Research Program

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, comprising more than 125 principal investigators, located in Maryland and at the Rocky Mountain Laboratories (RML) in Montana, who lead a wide range of basic, translational, and clinical research efforts; 2) the NIAID VRC, which conducts basic and translational research to facilitate the development of effective vaccines and biologic therapies for human 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 breadth of activities and the ability to pivot research projects to focus on emerging infectious threats as they arise ensures that the NIAID IRP can immediately fill the gaps in knowledge required to inform public health measures to prevent the spread of disease.

NIAID researchers utilize animal models to evaluate concepts critical to the implementation of public health measures. Understanding how a virus predominately spreads is important to reduce transmission between humans. For example, researchers at RML used a Syrian hamster animal model to evaluate the efficiency of airborne and contaminated surface contact to transmit SARS-CoV-2. Results from these studies showed that although SARS-CoV-2 replicated in the lungs regardless of exposure route, aerosol-exposed animals had more severe lung damage than their counterparts exposed only to contaminated surfaces. Additionally, airborne transmission was much more efficient at infecting animals, providing critical information to support guidance on reducing indoor airborne transmission of SARS-CoV-2 through masking, increased air filtration, and social distancing. As the effects of the COVID-19 pandemic endure and variants of concern continue to emerge, scientists in the NIAID IRP are continuing to inform and enhance vaccination and treatment strategies. VRC scientists and their collaborators completed a study in rhesus macaques to determine the impact on protection from COVID-19 of a booster shot of the mRNA-1273 vaccine six months after the primary series. Results showed that a booster of the original version of the vaccine or a slightly modified version targeting the beta variant of SARS-CoV-2 led to an increase in neutralizing antibody levels and provided protection against infection. The knowledge gained from this work supported the implementation of vaccine boosters to protect individuals from severe COVID-19. To support the development and optimization of COVID-19 treatment strategies, researchers at the NIAID Integrated Research Facility at Ft. Detrick are supporting efforts, sponsored by the HHS COVID Therapeutics Response Team, to test antibody therapeutics, small-molecule clinical candidates, and products with FDA Emergency Use Authorization (EUA) in cellular assays and in hamster infection models. These experimental and EUA therapies are tested against selected SARS-CoV-2 variants of concern to inform pharmacokinetic analysis and clinical efficacy. Data from these studies are shared with the manufacturers for inclusion in regulatory reporting and with the HHS COVID Therapeutics Response Team for internal decision-making and risk assessment as the variant landscape evolves.

As the effects of the COVID-19 pandemic continue to evolve, strategies are needed to assess the burden of disease across populations. To support this effort, NIAID researchers developed an algorithm to differentiate individuals who had a previous infection, a vaccination, or were unexposed to SARS-CoV-2. This algorithm proved very sensitive and specific and was used to evaluate seroprevalence and vaccination status trends among emergency department patients in an urban area over time. The results showed differences among ethnic groups and genders in both disease burden and vaccination status and could be applied to help address health disparities.

Budget Policy:
The FY 2024 President's Budget request for Intramural Research is $861.5 million, an increase of $8.5 million or 1.0 percent compared with the FY 2023 enacted level. The FY 2024 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 for the review, award, and monitoring of research grants, training awards, and research and development contracts. RMS activities include strategic planning and facilitation and evaluation of Institute programs, such as the NIAID International Centers of Excellence in Malaria Research (ICEMR) program. ICEMR is a global network of independent research centers in malaria-endemic settings that generates knowledge, tools, and evidence-based strategies crucial to understanding, controlling, and ultimately preventing malaria. NIAID'S Policy, Planning, and Evaluation (PP&E) Branch performed a multi-method evaluation of ICEMR to assess program outcomes and identify areas of improvement. The key findings of this evaluation included identifying substantial contributions made to malaria research by ICEMR, benefits of the program to junior investigators, and benefits and challenges of data sharing and collaborations for participating investigators; as well as capturing suggested emerging research trends to focus on in the future to advance the field. This information was incorporated into the development of the next iteration of the ICEMR program to optimize research outcomes. RMS activities also encompass regulatory compliance, international coordination, and liaison activities with other federal agencies, Congress, and the public.

Budget Policy:
The FY 2024 President's Budget request for RMS is $422.1 million, an increase of $4.2 million or 1.0 percent compared with the FY 2023 enacted level. This budget increase will mostly maintain the overall level of program management and administrative support.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	$6,322,728,000
Rescission				$0
2023	$6,268,313,000	$6,642,608,000	$6,449,804,000	$6,562,279,000
Rescission				$0
2024	$6,561,652,000			

[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	2023 Amount Authorized	FY 2023 Enacted	2024 Amount Authorized	FY 2024 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$6,561,652,000	Indefinite	$6,561,652,000
National Institute of Allergy and Infectious Diseases	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$6,561,652,000		$6,561,652,000

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National Institute of Allergy and Infectious Diseases

Amounts Available for Obligation [1]

(Dollars in Thousands)

Source of Funding	FY 2022 Final	FY 2023 Enacted	FY 2024 President's Budget
Appropriation	$6,322,728	$6,562,279	$6,561,652
Secretary's Transfer	$0	$0	$0
OAR HIV/AIDS Transfers	-$548	-$627	$0
Subtotal, adjusted budget authority	$6,322,180	$6,561,652	$6,561,652
Unobligated balance, start of year	$0	$0	$0
Unobligated balance, end of year (carryover)	$0	$0	$0
Subtotal, adjusted budget authority	**$6,322,180**	**$6,561,652**	**$6,561,652**
Unobligated balance lapsing	-$100	$0	$0
Total obligations	$6,322,080	$6,561,652	$6,561,652

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:
FY 2022 - $32,914 FY 2023 - $40,000 FY 2024 - $40,000

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Budget Authority by Object Class[1]
(Dollars in Thousands)

		FY 2023 Enacted	FY 2024 President's Budget	FY 2024 +/- FY 2023
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	$212	$223	$11
	Average GM/GS grade	12.7	12.7	0.0
	Average GM/GS salary	$129	$136	$7
	Average salary, Commissioned Corps (42 U.S.C. 207)	$108	$114	$5
	Average salary of ungraded positions	$168	$176	$8
	OBJECT CLASSES	**FY 2023 Enacted**	**FY 2024 President's Budget**	**FY 2024 +/- FY 2023**
	Personnel Compensation			
11.1	Full-Time Permanent	$208,131	$219,484	$11,352
11.3	Other Than Full-Time Permanent	$86,493	$91,210	$4,718
11.5	Other Personnel Compensation	$14,703	$15,505	$802
11.7	Military Personnel	$4,511	$4,757	$246
11.8	Special Personnel Services Payments	$27,876	$29,396	$1,520
11.9	**Subtotal Personnel Compensation**	**$341,714**	**$360,353**	**$18,639**
12.1	Civilian Personnel Benefits	$113,795	$119,492	$5,697
12.2	Military Personnel Benefits	$1,529	$1,612	$83
13.0	Benefits to Former Personnel	$0	$0	$0
	Subtotal Pay Costs	**$457,038**	**$481,457**	**$24,419**
21.0	Travel & Transportation of Persons	$4,598	$4,397	-$201
22.0	Transportation of Things	$1,976	$1,922	-$55
23.1	Rental Payments to GSA	$0	$0	$0
23.2	Rental Payments to Others	$0	$0	$0
23.3	Communications, Utilities & Misc. Charges	$1,922	$1,763	-$159
24.0	Printing & Reproduction	$11	$11	$0
25.1	Consulting Services	$208,252	$208,449	$197
25.2	Other Services	$192,604	$187,651	-$4,953
25.3	Purchase of Goods and Services from Government Accounts	$634,431	$631,461	-$2,970
25.4	Operation & Maintenance of Facilities	$10,463	$9,889	-$574
25.5	R&D Contracts	$824,254	$821,094	-$3,161
25.6	Medical Care	$6,786	$6,700	-$86
25.7	Operation & Maintenance of Equipment	$32,138	$30,222	-$1,916
25.8	Subsistence & Support of Persons	$2	$3	$0
25.0	**Subtotal Other Contractual Services**	**$1,908,931**	**$1,895,469**	**-$13,462**
26.0	Supplies & Materials	$57,103	$55,690	-$1,413
31.0	Equipment	$30,974	$29,211	-$1,763
32.0	Land and Structures	$6,595	$6,753	$158
33.0	Investments & Loans	$0	$0	$0
41.0	Grants, Subsidies & Contributions	$4,092,429	$4,084,905	-$7,524
42.0	Insurance Claims & Indemnities	$0	$0	$0
43.0	Interest & Dividends	$74	$74	$0
44.0	Refunds	$0	$0	$0
	Subtotal Non-Pay Costs	**$6,104,614**	**$6,080,195**	**-$24,419**
	Total Budget Authority by Object Class	**$6,561,652**	**$6,561,652**	**$0**

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

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Salaries and Expenses

(Dollars in Thousands)

Object Classes	FY 2023 Enacted	FY 2024 President's Budget	FY 2024 +/- FY 2023
Personnel Compensation			
Full-Time Permanent (11.1)	$208,131	$219,484	$11,352
Other Than Full-Time Permanent (11.3)	$86,493	$91,210	$4,718
Other Personnel Compensation (11.5)	$14,703	$15,505	$802
Military Personnel (11.7)	$4,511	$4,757	$246
Special Personnel Services Payments (11.8)	$27,876	$29,396	$1,520
Subtotal, Personnel Compensation (11.9)	**$341,714**	**$360,353**	**$18,639**
Civilian Personnel Benefits (12.1)	$113,795	$119,492	$5,697
Military Personnel Benefits (12.2)	$1,529	$1,612	$83
Benefits to Former Personnel (13.0)	$0	$0	$0
Subtotal Pay Costs	**$457,038**	**$481,457**	**$24,419**
Travel & Transportation of Persons (21.0)	$4,598	$4,397	-$201
Transportation of Things (22.0)	$1,976	$1,922	-$55
Rental Payments to Others (23.2)	$0	$0	$0
Communications, Utilities & Misc. Charges (23.3)	$1,922	$1,763	-$159
Printing & Reproduction (24.0)	$11	$11	$0
Other Contractual Services			
Consultant Services (25.1)	$208,252	$208,449	$197
Other Services (25.2)	$192,604	$187,651	-$4,953
Purchase of Goods and Services from Government Accounts (25.3)	$469,456	$466,486	-$2,970
Operation & Maintenance of Facilities (25.4)	$10,463	$9,889	-$574
Operation & Maintenance of Equipment (25.7)	$32,138	$30,222	-$1,916
Subsistence & Support of Persons (25.8)	$2	$3	$0
Subtotal Other Contractual Services	**$912,916**	**$902,701**	**-$10,215**
Supplies & Materials (26.0)	$57,103	$55,690	-$1,413
Subtotal Non-Pay Costs	**$978,527**	**$966,484**	**-$12,044**
Total Administrative Costs	**$1,435,565**	**$1,447,941**	**$12,376**

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Detail of Full-Time Equivalent Employment (FTE)

Office	FY 2022 Final			FY 2023 Enacted			FY 2024 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Clinical Research									
Direct:	94	5	99	95	5	100	95	5	100
Total:	94	5	99	95	5	100	95	5	100
Division of Extramural Activities									
Direct:	241	2	243	262	2	264	262	2	264
Total:	241	2	243	262	2	264	262	2	264
Division of Intramural Research									
Direct:	744	8	752	765	8	773	765	8	773
Total:	744	8	752	765	8	773	765	8	773
Office of the Director									
Direct:	431	1	432	446	1	447	446	1	447
Total:	431	1	432	446	1	447	446	1	447
Division of Allergy, Immunology, and Transplantation									
Direct:	101	1	102	101	1	102	101	1	102
Total:	101	1	102	101	1	102	101	1	102
Division of Microbiology and Infectious Diseases									
Direct:	185	7	192	199	7	206	199	7	206
Total:	185	7	192	199	7	206	199	7	206
Division of Acquired Immunodeficiency									
Direct:	155	4	159	166	4	170	166	4	170
Total:	155	4	159	166	4	170	166	4	170
Vaccine Research Center									
Direct:	118	2	120	116	2	118	116	2	118
Total:	118	2	120	116	2	118	116	2	118
Total	2,069	30	2,099	2,150	30	2,180	2,150	30	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
2020	12.6
2021	12.6
2022	12.7
2023	12.7
2024	12.7

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Detail of Positions [1]

GRADE	FY 2022 Final	FY 2023 Enacted	FY 2024 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	$407,400	$424,205	$445,628
General Schedule			
GM/GS-15	210	215	218
GM/GS-14	429	448	445
GM/GS-13	424	431	435
GS-12	250	264	259
GS-11	126	126	134
GS-10	1	1	1
GS-9	71	79	74
GS-8	24	26	26
GS-7	43	52	49
GS-6	11	11	12
GS-5	5	4	4
GS-4	5	8	8
GS-3	6	6	6
GS-2	0	1	1
GS-1	2	3	3
Subtotal	1,607	1,675	1,675
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	9	9	9
Senior Grade	7	8	8
Full Grade	7	9	8
Senior Assistant Grade	6	4	4
Assistant Grade	0	0	0
Co-Step	1	0	1
Subtotal	30	30	30
Ungraded	490	509	509
Total permanent positions	1,627	1,620	1,620
Total positions, end of year	2,129	2,216	2,216
Total full-time equivalent (FTE) employment, end of year	2,099	2,180	2,180
Average ES salary	$203,700	$212,103	$222,814
Average GM/GS grade	12.7	12.7	12.7
Average GM/GS salary	$124,105	$129,225	$135,751