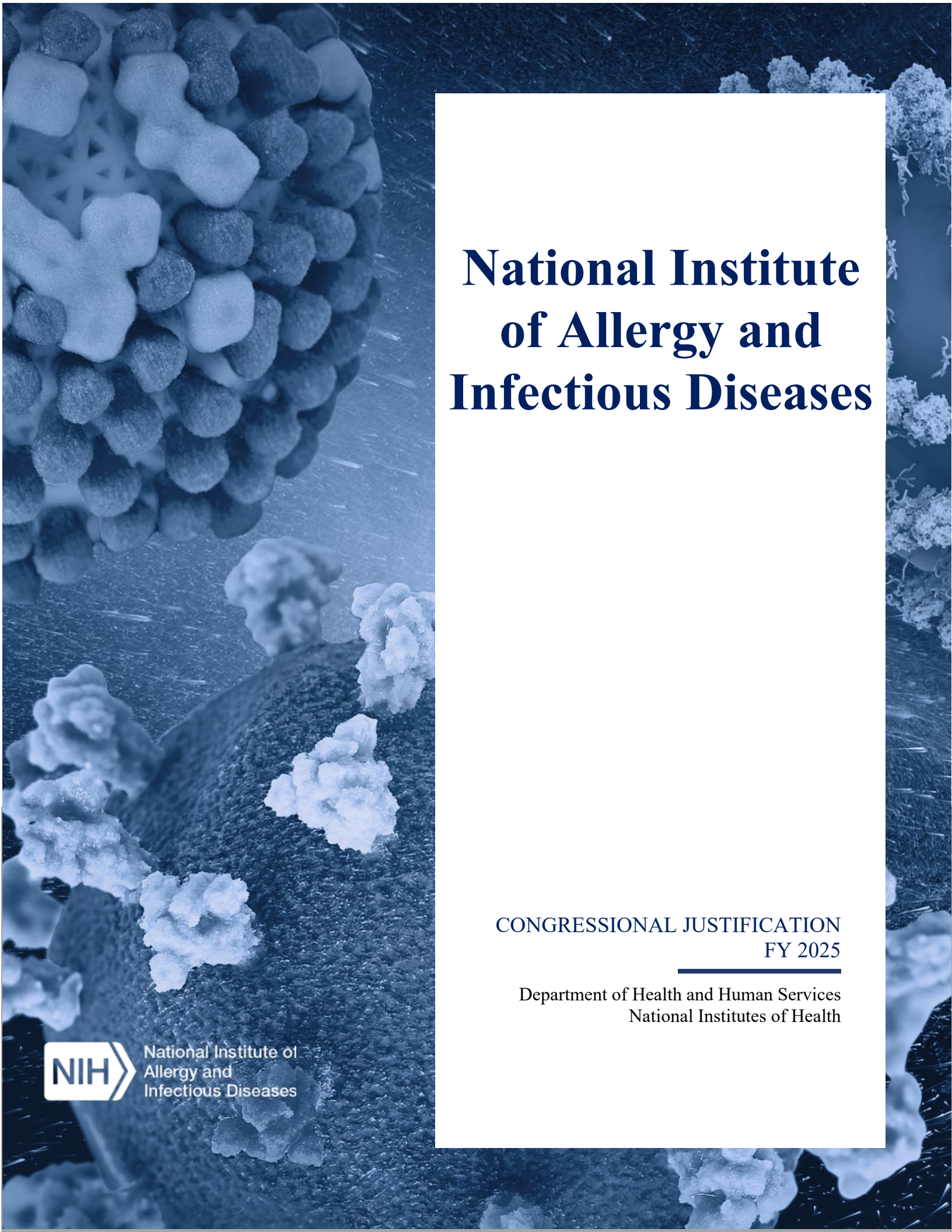

National Institute of Allergy and Infectious Diseases

CONGRESSIONAL JUSTIFICATION
FY 2025

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)

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General Notes

1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

Cover Page

Creative work featuring 3D renditions of three dangerous respiratory viruses: RSV (top right), SARS-CoV-2 (bottom center), and influenza (top left). Note: not to scale. Credit: NIAID

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Director's Overview

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports biomedical research to better understand, treat, and prevent infectious and immune-mediated diseases. For more than 65 years, NIAID research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States (U.S.) and worldwide. NIAID manages a complex and comprehensive research portfolio that aims to expand the breadth and depth of knowledge in its mission areas. As part of its mandate, NIAID also leads the research response to emerging and re-emerging disease threats by leveraging research capacities both within the U.S. and around the globe.

Jeanne Marrazzo, M.D., M.P.H.
NIAID Director

NIAID is a global leader in the effort to combat the HIV/AIDS pandemic, one of humanity's deadliest and most persistent epidemics. This year marks the 20th anniversary of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), a transformational U.S. government initiative aimed at preventing, treating, and caring for people living with HIV and AIDS. Over the past two decades, NIAID research has played a pivotal role in demonstrating the effectiveness of interventions offered through PEPFAR. NIAID-supported programs, including the International epidemiology Databases to Evaluate AIDS (IeDEA) Cohort Consortium and the Centers for AIDS Research (CFAR), have been foundational in providing harmonized data sets and supporting the identification of strategies to treat and prevent HIV. NIAID research continues to inform best practices recommended by the World Health Organization (WHO) for preventing HIV. This includes the critical role of early initiation of antiretroviral therapy (ART) in reducing HIV transmission, the optimization of drug regimens to prevent mother-to-child transmission, and the important role of health practices, such as male circumcision, in reducing HIV acquisition. NIAID research also has been pivotal in the optimization of ART regimens, transforming HIV infection from an almost uniformly fatal infection into a manageable chronic condition.

When COVID-19 emerged as a global public health threat, NIAID was at the forefront of the immediate public health response that led to the development of effective vaccine strategies. NIAID is continuing to advance SARS-CoV-2 research including addressing the detrimental longer-term sequelae of SARS-CoV-2 infection. One example of this effort is the Pandemic Autopsy Study, in which scientists performed autopsies on individuals who died from COVID-19 in the first year of the pandemic to determine where in the body SARS-CoV-2 infects and persists. Findings from this study were critical in providing the rationale for a clinical study of the antiviral drug, Paxlovid, for treating Long COVID. NIAID also continues to support research to evaluate the long-term impacts of COVID-19 in children, including multisystem inflammatory syndrome in children (MIS-C). The Pediatric SARS-CoV-2 MIS-C Long-term Outcomes Study, or PECOS, established a cohort of pediatric patients with symptomatic and

asymptomatic SARS-CoV-2 infection to study the long-term sequelae of acute infection and the evolution of the immune response over time.

In addressing ongoing public health threats, NIAID continues to advance research and technology to develop more effective vaccines. NIAID and the Biomedical Advanced Research and Development Authority (BARDA) are leading the U.S. Department of Health and Human Services (HHS) initiative, "Project NextGen," which prioritizes the development of next-generation COVID-19 vaccines, such as those with enhanced breadth of protection to SARS-CoV-2 variants, improved durability, and enhanced ability to block infection or transmission. A key strategy for improving vaccine efficacy is the development of mucosal vaccines. Like other respiratory viruses, SARS-CoV-2 enters the body and infects through the mucosal tissue of the respiratory tract. Vaccines developed to promote an immune response at the mucosal surface may be better at blocking infection than traditional vaccines. In April 2023, NIAID published a workshop report summarizing key scientific gaps in and opportunities for advancing mucosal vaccine research. The workshop was a joint effort between NIAID, the Coalition for Epidemic Preparedness Innovation, the Bill and Melinda Gates Foundation, BARDA, and the Wellcome Trust. Advances in mucosal vaccine development could lead to improved vaccines for other public health challenges, including respiratory syncytial virus (RSV), tuberculosis, and influenza. Moreover, NIAID is supporting clinical trials of promising next-generation vaccines for influenza, which could provide broad protection against many subtypes of influenza, negate the need for an annual influenza vaccine, and potentially prevent an influenza pandemic.

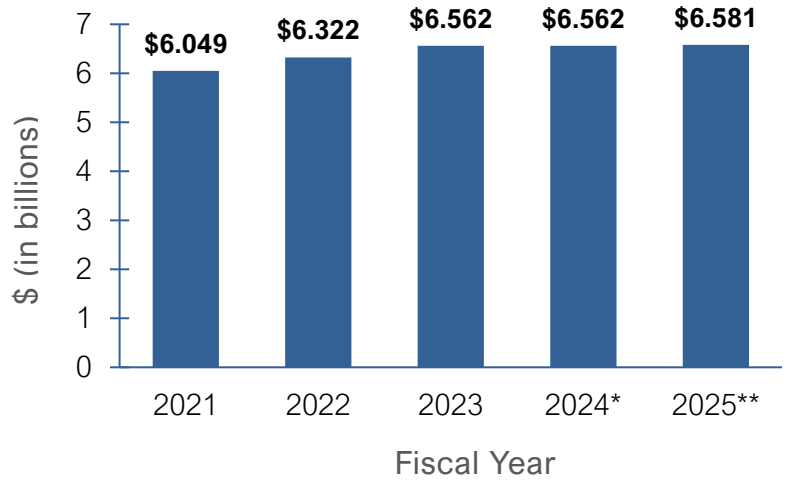
NIAID is committed to prioritizing diversity as an essential element of optimizing the global biomedical research community. NIAID continues to prioritize support of an extramural research portfolio inclusive of the diverse populations it serves and works to enhance efforts to address health disparities, health equity and better understand the social determinants of health.

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 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.

FUNDING HISTORY



*Under Continuing Resolution

**President's budget request

Director Profile: Jeanne Marrazzo, M.D., M.P.H., is the Director of NIAID. She began her tenure at NIAID in September 2023 after serving as the Director of the Division of Infectious Diseases at the University of Alabama at Birmingham. Dr. Marrazzo's research focuses on HIV prevention and prevention and management of sexually transmitted infections.

FACTS AND FIGURES

FULL TIME EQUIV. EMPLOYEES	2,064
FUNDED PRINCIPAL INVESTIGATORS	1,333

Averaged over FY 2020-FY 2023

RESEARCH HIGHLIGHTS

Lenacapavir, a new long-acting HIV antiviral drug targeting the HIV-1 capsid, received FDA breakthrough therapy designation, expediting its development and review. Fundamental science conducted at NIAID structural biology centers provided the foundation for the development of lenacapavir.

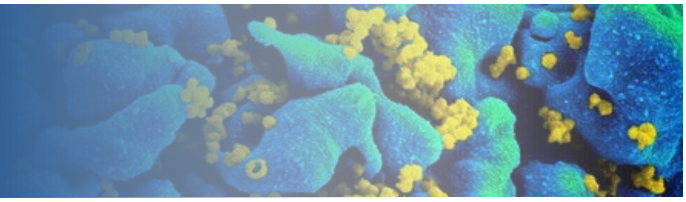
NIAID researchers have developed human tonsil organoids to examine immune responses to influenza vaccine candidates and adjuvants. Tonsil organoids are useful for defining essential cellular components of a vaccine response, and they provide a platform for testing in a non-animal model.

Chikungunya virus (CHIKV) is a member of a group of mosquito-borne viruses that cause musculoskeletal disease (arthritogenic alphaviruses). NIAID-supported researchers showed that a CHIKV vaccine induced protective antibodies against CHIKV in humans, and the protection extended to other alphaviruses.

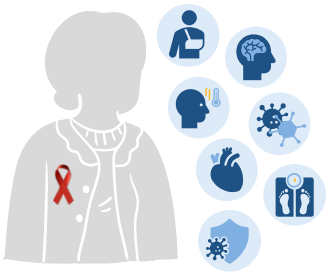
An NIAID-funded study showed a two-thirds reduction in the incidence of syphilis, gonorrhea, and chlamydia among men who have sex with men and transgender women when the oral antibiotic, doxycycline, was taken within 72 hours after unprotected sex.

NIAID scientists have developed an innovative COVID-19 vaccine for children that can be given as a single dose nasal spray. The vaccine offers protection against SARS-CoV-2 and human parainfluenza virus 3 – another viral cause of respiratory illness in children – and is proceeding to a Phase 1 clinical trial.

National Institute of Allergy and Infectious Diseases

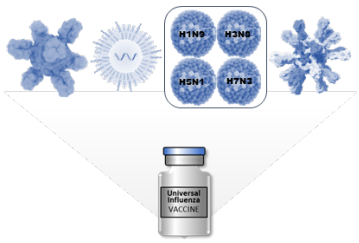


RESEARCH ADVANCES



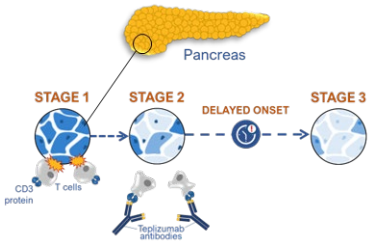
Multimorbidity is common in older people with HIV (PWH). NIH studies are evaluating the intersection of age, co-infections, inflammation, and immune function and exploring interventions to prevent and treat these comorbidities.

- The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study, which was a joint effort between NIAID and NHLBI, found that the lipid lowering medication, pitavastatin, reduced major cardiovascular events by more than 30 percent in PWH.
- NIAID-supported IeDEA studies are examining the epidemiology of non-communicable diseases and aging among PWH on antiretroviral therapy, specifically focused on cardiovascular risk factors, mental health, substance use, and liver diseases.



Current flu vaccines can limit the severity of influenza, but they do not work against every flu strain and must be taken yearly. A **universal flu vaccine** could protect against a wide variety of strains and provide long-term immunity, eliminating the need for people to get an annual flu shot. Examples of progress towards this goal include:

- In May 2023, NIAID began a clinical trial of an H1ssF mRNA vaccine, testing its safety and ability to induce an immune response. The vaccine targets the slowly evolving stem part of the HA surface protein on the influenza virus.
- Results are expected in FY 2024 for a NIAID-supported clinical trial evaluating vaccine candidate, BPL-1357, a whole-virus vaccine made up of four strains of non-infectious, chemically inactivated, low-pathogenicity avian flu virus.



Type 1 diabetes (T1D) is a life-threatening autoimmune disease that requires individuals to take insulin for the rest of their lives. **FDA recently approved two T1D therapies**, both of which originated from long-standing NIAID- and NIDDK-funded research efforts.

- In November 2022, FDA approved teplizumab, an antibody that delays T1D onset, after decades of NIH, academic, and industry investment in T1D research.
- In June 2023, FDA approved Lantidra, the first Purified Human Pancreatic Islet (PHPI) therapy, for treating T1D. The NIH Clinical Islet Transplantation consortium, a joint NIAID and NIDDK program, conducted critical Phase 3 clinical trials evaluating PHPI efficacy.

Selected Future Research Initiatives

- **HIV CURE IN DIVERSE POPULATIONS.** Supporting HIV cure-related research in diverse cohorts of people living with HIV to determine similarities and differences in the establishment and dynamics of persistent viral reservoirs.
- **INFLUENZA IMMUNITY.** Employing computational modeling to advance understanding of the requirements for improving anti-influenza immunity.
- **ANTIBIOTIC RESISTANCE.** Supporting research to develop tools and countermeasures for rapid identification and treatment of antibiotic resistant infections.
- **TICKBORNE DISEASES.** Expanding understanding of potential immune evasion mechanisms of tickborne pathogens that contribute to human disease and death.

NIAID Commitment to Diversity, Equity, Inclusion, and Accessibility (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 2025 President's Budget request for the National Institute of Allergy and Infectious Diseases (NIAID) is $6,581.3 million, an increase of $19.6 million or 0.3 percent compared to the FY 2023 Final 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) (+$91.0 million; total $3,824.5 million):
NIAID will support a total of 5,450 RPG awards in FY 2025. 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 increase by $47.5 million or 6.1 percent in FY 2025, while noncompeting RPG funding will increase by $51.0 million or 1.9 percent. Overall RPG funding will increase by 2.4 percent.

Other Research (+$5.7 million, total $107.3 million):
NIAID will increase Other Research funding by 5.6 percent compared with the FY 2023 Final level. NIAID will continue to support the research resources needed to prevent, prepare for, and respond to infectious disease outbreaks.

Research and Development Contracts (R&D) (-$119.6 million; total $1,161.6 million):
NIAID will continue to support trans-NIH initiatives, including ongoing cybersecurity efforts, as well as other HHS-wide initiatives. Overall R&D Contract funding will decrease by 9.3 percent to realign resources to support high priority research initiatives, such as maintaining a robust investigator-initiated grant portfolio while covering mandatory cost increases in other mechanisms.

Intramural Research (IR) (+$23.6 million; total $879.9 million):
NIAID will continue to support critical long-range priorities with funds carefully aligned to key research on infectious diseases, such as HIV/AIDS, respiratory syncytial virus (RSV), malaria, influenza, antimicrobial resistance/combatting antibiotic-resistant bacteria (CARB), and vector-borne diseases. Funding will also support the proposed FY 2025 pay increase for intramural research employees.

Research Management and Support (RMS) (+$17.3 million; total $436.0 million):
NIAID will increase funding for RMS by 4.1 percent. This budget will support ongoing program management and administrative support. Funding will also support the proposed FY 2025 pay increase.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Budget Mechanism *

(Dollars in Thousands)

Mechanism	FY 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Research Projects:								
Noncompeting	3,434	$2,754,022	3,599	$2,758,118	3,683	$2,805,034	249	$51,013
Administrative Supplements	*(181)*	$24,047	*(181)*	$24,047	*(181)*	$24,047	*(0)*	$0
Competing:								
Renewal	161	$117,291	172	$125,943	170	$125,083	9	$7,791
New	1,244	$658,133	1,326	$702,433	1,317	$697,841	73	$39,708
Supplements	0	$0	0	$0	0	$0	0	$0
Subtotal, Competing	**1,405**	**$775,425**	**1,498**	**$828,376**	**1,487**	**$822,924**	**82**	**$47,499**
Subtotal, RPGs	4,839	$3,553,494	5,097	$3,610,541	5,170	$3,652,006	331	$98,512
SBIR/STTR	292	$180,045	280	$172,539	280	$172,539	-12	-$7,506
Research Project Grants	5,131	$3,733,539	5,377	$3,783,081	5,450	$3,824,545	319	$91,006
Research Centers								
Specialized/Comprehensive	37	$101,181	37	$101,181	37	$101,716	0	$535
Clinical Research	0	$0	0	$0	0	$0	0	$0
Biotechnology	0	$0	0	$0	0	$0	0	$0
Comparative Medicine	0	$500	0	$500	0	$500	0	$0
Research Centers in Minority Institutions	0	$0	0	$0	0	$0	0	$0
Research Centers	**37**	**$101,681**	**37**	**$101,681**	**37**	**$102,216**	**0**	**$535**
Other Research:								
Research Careers	292	$49,801	293	$50,498	297	$51,205	5	$1,404
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	$232	0	$0
Other	123	$51,507	134	$55,827	134	$55,827	11	$4,319
Other Research	**415**	**$101,540**	**427**	**$106,557**	**431**	**$107,264**	**16**	**$5,724**
Total Research Grants	5,583	$3,936,760	5,841	$3,991,318	5,918	$4,034,025	335	$97,265
Ruth L Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	260	$12,251	260	$12,422	263	$12,596	3	$345
Institutional Awards	915	$56,383	915	$57,172	915	$57,172	0	$789
Total Research Training	**1,175**	**$68,634**	**1,175**	**$69,594**	**1,178**	**$69,768**	**3**	**$1,135**
Research & Develop. Contracts	224	$1,281,252	204	$1,200,631	194	$1,161,607	-30	-$119,645
SBIR/STTR (non-add)	*(25)*	*($20,053)*	*(25)*	*($20,053)*	*(25)*	*($20,053)*	*(0)*	*($0)*
Intramural Research	947	$856,326	991	$871,167	991	$879,879	44	$23,553
Res. Management & Support	1,162	$418,681	1,189	$429,568	1,189	$436,012	27	$17,331
SBIR Admin. (non-add)		*($1,476)*		*($2,100)*		*($2,100)*		*($624)*
Construction		$0		$0		$0		$0
Buildings and Facilities		$0		$0		$0		$0
Total, NIAID	**2,109**	**$6,561,652**	**2,180**	**$6,562,279**	**2,180**	**$6,581,291**	**71**	**$19,639**

* 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, $6,581,291,000.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

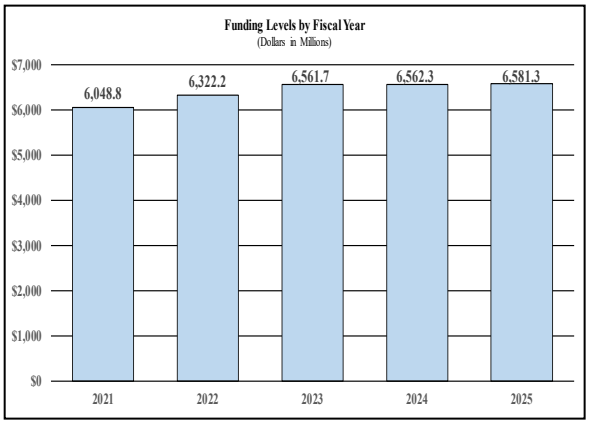
Summary of Changes
(Dollars in Thousands)

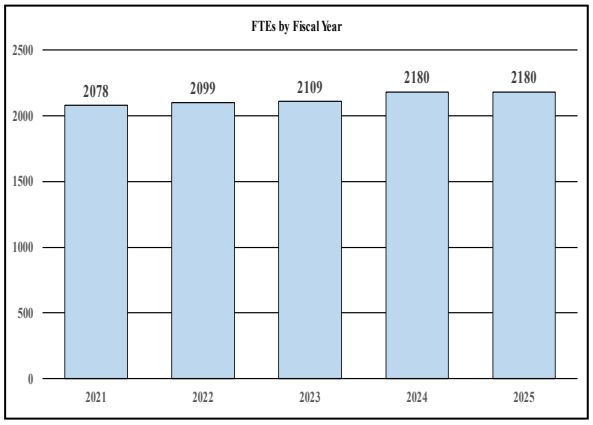
CHANGES	FY 2023 Final FTEs	FY 2023 Final Budget Authority	FY 2025 President's Budget FTEs	FY 2025 President's Budget Budget Authority	Built-In Change from FY 2023 Final FTEs	Built-In Change from FY 2023 Final Budget Authority
1. Intramural Research:						
A. Built-in cost changes:						
a. FY 2024 effect of FY 2023 pay & benefits increase		$215,358		$244,720		$2,541
b. FY 2024 effect of FY 2024 pay & benefits increase		$215,358		$244,720		$8,380
c. FY 2024 paid days adjustment		$215,358		$244,720		$829
d. Differences attributable to FY 2024 change in FTE		$215,358		$244,720		$10,006
e. FY 2025 effect of FY 2024 pay & benefits increase		$215,358		$244,720		$2,973
f. FY 2025 effect of FY 2025 pay & benefits increase		$215,358		$244,720		$4,043
g. FY 2025 paid days adjustment		$215,358		$244,720		$0
h. Differences attributable to FY 2025 change in FTE		$215,358		$244,720		$0
i. Payment for centrally furnished services		$115,962		$124,340		$8,379
j. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		$525,006		$510,818		$35,209
Subtotal, IR built-in cost changes						$72,359
2. Research Management and Support:						
A. Built-in cost changes:						
a. FY 2024 effect of FY 2023 pay & benefits increase		$226,342		$250,314		$2,676
b. FY 2024 effect of FY 2024 pay & benefits increase		$226,342		$250,314		$8,806
c. FY 2024 paid days adjustment		$226,342		$250,314		$871
d. Differences attributable to FY 2024 change in FTE		$226,342		$250,314		$5,259
e. FY 2025 effect of FY 2024 pay & benefits increase		$226,342		$250,314		$3,031
f. FY 2025 effect of FY 2025 pay & benefits increase		$226,342		$250,314		$4,181
g. FY 2025 paid days adjustment		$226,342		$250,314		$0
h. Differences attributable to FY 2025 change in FTE		$226,342		$250,314		$0
i. Payment for centrally furnished services		$22,822		$24,471		$1,649
j. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		$169,406		$161,226		$11,035
Subtotal, RMS built-in cost changes						$37,509

CHANGES	FY 2023 Final No.	FY 2023 Final Amount	FY 2025 President's Budget No.	FY 2025 President's Budget Amount	Program Change from FY 2023 Final No.	Program Change from FY 2023 Final Amount
B. Program:						
1. Research Project Grants:						
a. Noncompeting	3,434	$2,778,069	3,683	$2,829,081	249	$51,013
b. Competing	1,405	$775,425	1,487	$822,924	82	$47,499
c. SBIR/STTR	292	$180,045	280	$172,539	-12	-$7,506
Subtotal, RPGs	5,131	$3,733,539	5,450	$3,824,545	319	$91,006
2. Research Centers	37	$101,681	37	$102,216	0	$535
3. Other Research	415	$101,540	431	$107,264	16	$5,724
4. Research Training	1,175	$68,634	1,178	$69,768	3	$1,135
5. Research and development contracts	224	$1,281,252	194	$1,161,607	-30	-$119,645
Subtotal, Extramural		$5,286,646		$5,265,400		-$21,245
6. Intramural Research	947	$856,326	991	$879,879	44	-$48,806
7. Research Management and Support	1,162	$418,681	1,189	$436,012	27	-$20,178
8. Construction		$0		$0		$0
9. Buildings and Facilities		$0		$0		$0
Subtotal, program changes						-$90,229
Total built-in and program changes	2,109	$6,561,652	2,180	$6,581,291	71	$19,639

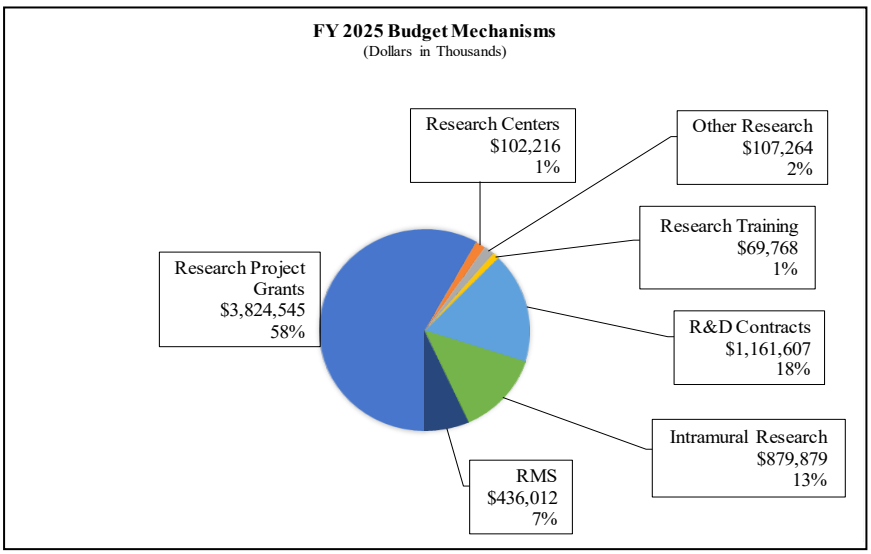
Fiscal Year 2025 Budget Graphs

History of Budget Authority and FTEs:

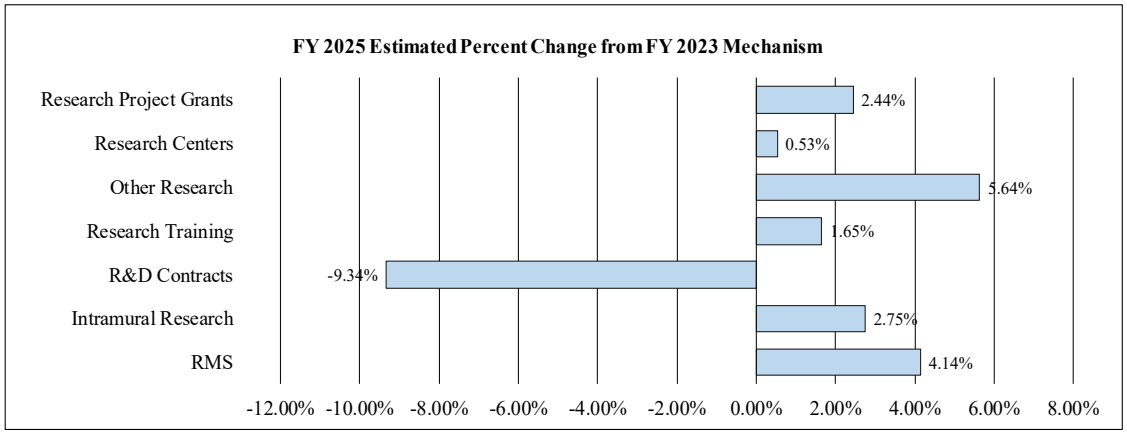




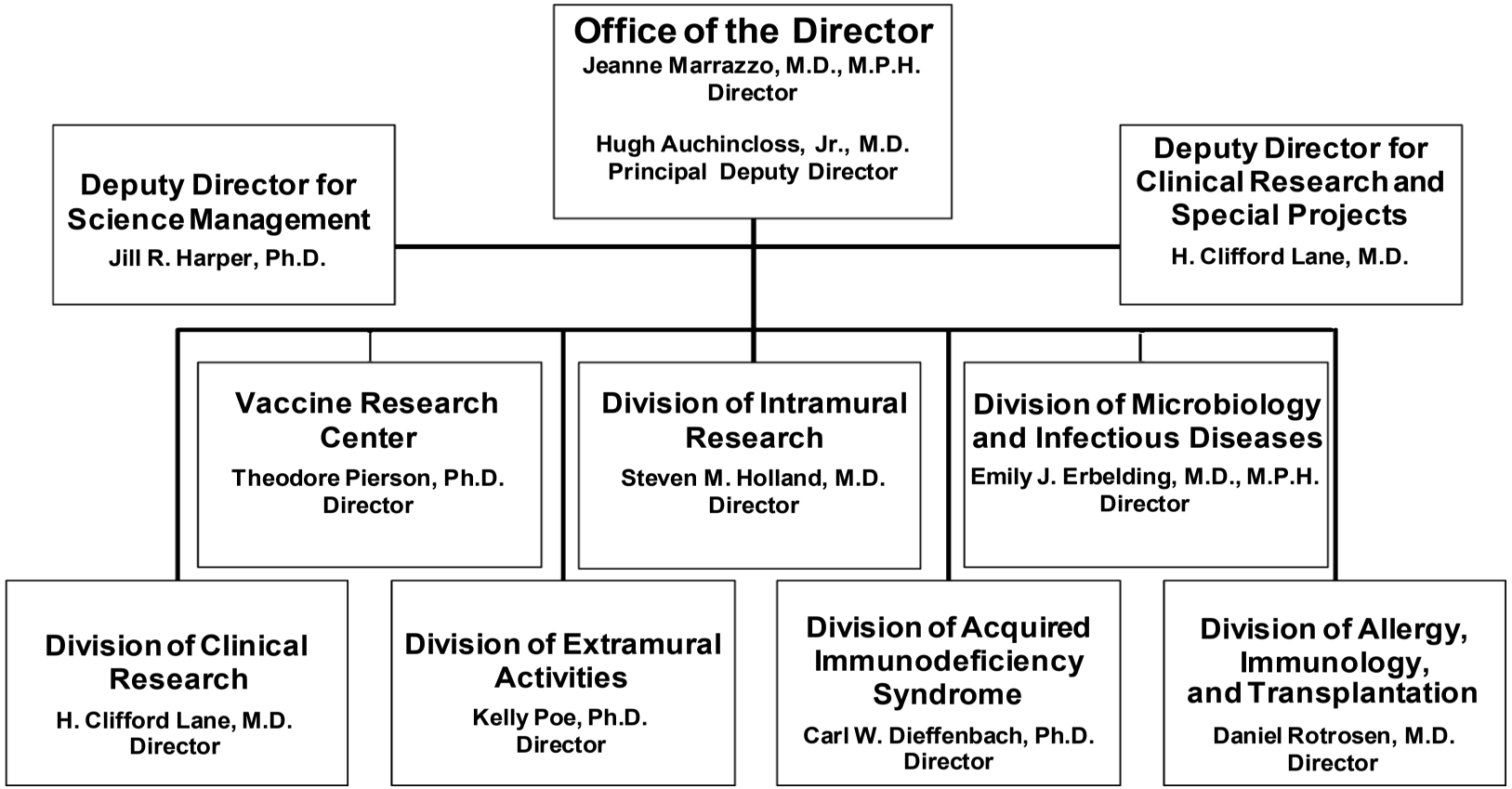
Distribution by Mechanism:



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 *
(Dollars in Thousands)

	FY 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023 Final	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
HIV/AIDS [1]		$1,533,969		$1,526,909		$1,521,706		-$12,263
Biodefense & Emerging Infectious Diseases		$2,209,732		$2,199,783		$2,199,856		-$9,875
Infectious & Immunological Diseases		$1,542,945		$1,534,852		$1,543,838		$893
Subtotal, Extramural		**$5,286,646**		**$5,261,544**		**$5,265,400**		**-$21,245**
Intramural Research	**947**	**$856,326**	**991**	**$871,167**	**991**	**$879,879**	**44**	**$23,553**
Research Management & Support	**1,162**	**$418,681**	**1,189**	**$429,568**	**1,189**	**$436,012**	**27**	**$17,331**
TOTAL	**2,109**	**$6,561,652**	**2,180**	**$6,562,279**	**2,180**	**$6,581,291**	**71**	**$19,639**

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

[1] Reflects NIAID extramural for HIV/AIDS. NIAID HIV/AIDS total is (in thousands) $1,911,364 in FY 2023; $1,911,991 in FY 2024; and $1,911,364 in FY 2025.

National Institute of Allergy and Infectious Diseases

Authorizing Legislation: *Section 301 and title IV of the PHS Act*

Budget Authority (BA):

	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget	FY 2025 +/- FY 2023
BA	$6,561,652,000	$6,562,279,000	$6,581,291,000	+$19,639,000
FTE	2,109	2,180	2,180	71

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

Overall Budget Policy:
The FY 2025 President's Budget request seeks annual funding to continue support of the dual mandate of the National Institute of Allergy and Infectious Diseases (NIAID) 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 2025 President's Budget request is $6,581.3 million, an increase of $19.6 million or 0.3 percent compared to the FY 2023 Final 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 continuing to advance research on SARS-CoV-2 infection.

The Institute remains focused on high priority areas of research such as other emerging infectious diseases, agents with bioterrorism potential, HIV/AIDS, respiratory syncytial virus (RSV), 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 2025, 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.

The FY 2025 request continues support for efforts to develop a universal influenza vaccine, trans-NIH initiatives, as well as other HHS-wide initiatives through the research and development contract mechanism. NIAID's Intramural Research Program (IRP) will continue support for critical long-range priorities with resources aligned to key research on infectious diseases such as HIV/AIDS, malaria, and influenza.

Program Descriptions

HIV/AIDS

Over the past several decades, advances in antiretroviral therapy (ART) regimens and treatment paradigms have substantially reduced morbidity and mortality resulting from HIV infection. Early detection and promotion of adherence to ART are proven strategies to mitigate HIV transmission; however, HIV/AIDS remains a global health crisis, with more than one million new infections occurring globally each year.[1] NIAID is a key component of the HHS initiative "Ending the HIV Epidemic in the United States" (EHE), which aims to reduce new HIV infections in the U.S. by 90 percent by 2030. Social and structural determinants of health, including poverty, stigma, and discrimination, combined with factors such as mental health and substance use disorders (i.e., alcohol, drug, and polysubstance), underlie and contribute to inequities in HIV prevention, linkage to care, and optimal uptake of ART. The EHE initiative works to address these inequities by prioritizing efforts in U.S. localities where more than 50 percent of new HIV diagnoses occur, as well as 7 states with a substantial rural HIV burden.

Multimorbidity in Older People with HIV

People living with HIV (PWH) experience age-related diseases earlier and at higher rates than those without HIV. To address this, NIAID supports research evaluating the intersection of age, co-infections, co-morbidities, inflammation, and immune function. The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study, a joint effort between NIAID and the National Heart, Lung, and Blood Institute (NHLBI), revealed that the lipid lowering medication, pitavastatin, reduced major cardiovascular events by more than 30 percent in PWH. Additional studies are in development to explore treatments for conditions such as vasomotor symptoms (hot flashes), frailty, obesity, and cardiovascular disease. Domestically, the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) is following more than 30,000 PWH and studying outcomes across multiple major systems: cardiovascular, lung, frailty, mental health, liver, kidney, and cancer. The Multicenter AIDS Cohort study and Women's Interagency HIV study Clinical Cohort Study (MWCCS), led by NHLBI with support from other NIH Institutes, Centers, and Offices (ICOs) including NIAID, conducts in-depth assessments of pathogenic mechanisms in aging and HIV using decades of clinical data and specimens. Globally, IeDEA is following more than 2.25 million PWH across 44 countries. One IeDEA study is examining the epidemiology of non-communicable diseases and aging among PWH on ART, specifically focused on cardiovascular risk factors, mental health, substance use, and liver diseases.

Efforts to end the HIV/AIDS pandemic will be greatly enhanced by the development of a safe and effective HIV vaccine. To advance this goal, NIAID supports high-impact, innovative research for HIV vaccine discovery. These efforts include the advancement and testing of promising technologies such as mRNA, nanoparticle, and vector-based vaccine candidates. In 2023, the NIAID-supported HIV Vaccine Trials Network (HVTN) launched a study to examine the safety and immunogenicity of three experimental mRNA vaccines. The HVTN also initiated a clinical trial examining an investigational T cell vaccine, called VIR-1388, that recognizes different parts, or epitopes, of HIV. VIR-1388 uses a viral vector, which researchers hope can deliver the vaccine immunogen so that the body would retain it for a prolonged period and overcome waning immunity seen with other vaccine strategies. Another NIAID-sponsored study is testing a nanoparticle-based vaccine candidate that displays multiple copies of HIV proteins arranged in a repetitive pattern to stimulate the immune system. This vaccine aims to coax B cells to produce broadly neutralizing

[1] who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics

antibodies (bNAbs), which can neutralize many HIV strains. Researchers are testing two different modes of delivery – a single injection given twice over three months and "fractionated" dosage, where the vaccine is given in six smaller amounts over three weeks – to determine the most effective administration. Additionally, NIAID is advancing innovative methods to recruit highly vulnerable persons for HIV vaccine studies through the application of mobile technology and social networking apps.

NIAID is investing in multiple approaches to prevent HIV in women, pregnant and postpartum people, infants, and children. The NIAID-supported International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) recently completed multiple studies showing that medications in commonly used ART regimens are safe and effective in adolescents (doravirine), pregnant people (dolutegravir), and postpartum individuals for perinatal transmission prevention (tenofovir alafenamide). IMPAACT network studies also were pivotal in lowering the age limit for use of dolutegravir to six months. Prior to this study, administration of dolutegravir was limited to adults and children weighing enough to take the adult tablet formulation. Additional IMPAACT studies resulted in the U.S. Food and Drug Administration (FDA) approval of an extended indication for Triumeq PD (abacavir, dolutegravir, and lamivudine) in children less than 12 years of age and demonstrated that long-acting ART was safe and effective in adolescents 12 to 18 years of age. NIAID also has supported several multipurpose prevention therapies (MPTs), products developed with multiple active drugs to simultaneously prevent HIV, other sexually-transmitted infections (STIs), or unintended pregnancy. Current promising MPTs supported by NIAID include an implant with potential to provide two years of contraception and pre-exposure prophylaxis (PrEP), and an easier-to-use long-acting injectable MPT to provide high-efficacy contraception with sustained PrEP.

One of the major NIAID priorities in HIV research is achieving a cure. One definition of a cure is controlling the HIV "reservoir," pockets of virus that lie dormant in certain cells in the body, without the need for continuous ART. To advance the goals of achieving an HIV cure, NIAID supports the Martin Delaney Collaboratories for HIV Cure Research program, which fosters multidisciplinary collaborations between basic, applied, and clinical researchers studying HIV persistence. As one strategy to target latent HIV, NIAID is evaluating several bNAbs that might be used either by themselves or in combination with compounds that reactivate latent HIV. A vaccine candidate supported by NIAID, Trimer 4571, is designed to stimulate the development of bNAbs to HIV and is being tested in early studies to evaluate whether it is safe, well-tolerated, and can induce the intended effects on the immune system. Another NIAID-supported study is investigating the safety, tolerability, and efficacy of N-803, a protein complex designed to reactivate latent HIV, with and without the addition of bNAbs. The goal of this combination approach is to enhance the body's ability to destroy reservoirs of HIV by both reactivating latent HIV and then inducing powerful immune responses to destroy infected cells. These studies mark progress towards the development of a cure for HIV.

Budget Policy:
The FY 2025 President's Budget request for the extramural component of the HIV/AIDS research is $1,521.7 million, which is a decrease of $12.3 million from the FY 2023 Final 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 2025 request sustains FY 2023 Final funding levels for the Centers for AIDS Research (CFAR) activities and similar efforts to support ongoing research in support of the Ending the HIV Epidemic in the U.S. (EHE) initiative. The Centers and related efforts offer evidence-based practices on prevention and treatment to initiative partners and support for evaluating the initiative.

Biodefense and Emerging Infectious Diseases

NIAID continues to be a leader in supporting biomedical research on emerging and re-emerging disease threats, including the persistent challenge of influenza. Each year, seasonal influenza sickens millions and leads to thousands of hospitalizations and flu-related deaths. Influenza can be particularly dangerous in children, immunocompromised people, and older adults, underscoring the need for vaccines that stimulate vigorous and long-lasting immune responses. NIAID-supported Collaborative Influenza Vaccine Innovation Centers (CIVICs) have developed animal models simulating vulnerable people, including aged, obese, type 1 diabetic, and pregnant animals. Through the CIVICs program, NIAID has advanced five novel influenza vaccine candidates into manufacturing for use in Phase 1 clinical trials planned through calendar year 2025. NIAID also is continuing research to improve currently available influenza vaccines with the addition of adjuvants, which can enhance the immune response. NIAID is assessing adjuvants in vaccines targeting a strain of highly pathogenic avian influenza virus that can infect humans, H5N8. In pre-clinical studies, the addition of an adjuvant to the H5N8 vaccines increased immune responses and resulted in significantly better immune protection compared to unadjuvanted versions.

Even though the immediate COVID-19 public health emergency has lessened, research to better understand the disease and improve medical countermeasures (MCMs) for SARS-CoV-2 is ongoing. For example, NIAID researchers evaluated potential allergic reactions associated with FDA-licensed COVID-19 mRNA vaccines and found that individuals who reported moderate to severe allergic reactions to their first dose of COVID-19 mRNA vaccines were able to safely tolerate subsequent doses. This finding may help individuals who are hesitant to receive a subsequent immunization after an initial allergic response to an mRNA COVID-19 vaccines. The Multisite Observational Maternal and Infant Study for COVID-19 (MOMI-Vax) study characterized the immune responses elicited by FDA-licensed COVID-19 mRNA vaccines in pregnant people. Participants received a primary two-dose series or the primary series plus a booster dose. Results from this study showed that vaccination during pregnancy produced robust immune responses and protective antibodies that were transferred to the newborn. Boosting during pregnancy significantly increased antibody concentration in the pregnant person's blood and antibodies transferred to the newborn supporting the addition of boosters during pregnancy. NIAID also is working to develop therapeutics to treat SARS-CoV-2 infection. NIAID, along with the National Center for Advancing Translational Sciences (NCATS), recently initiated a multi-site clinical trial evaluating an investigational antiviral known as S-217622. The trial is assessing whether S-217622 can improve clinical outcomes for patients who are hospitalized with COVID-19. This is the first agent to be evaluated in a new NIAID-funded global clinical research protocol known as Strategies and Treatments for Respiratory Infections & Viral

Emergencies (STRIVE), which can be adapted to rapidly assess multiple therapeutic interventions during outbreaks of respiratory diseases.

Filoviruses can cause severe hemorrhagic fever and are highly lethal, with notable recent outbreaks of Ebola virus, Sudan virus (SUDV), and Marburg virus (MARV). NIAID continues to prioritize research on developing vaccines and treatments for these re-emerging diseases of concern. In one study, NIAID researchers showed that an experimental vaccine, VSV-SUD, completely protected non-human primates (NHP) from developing SUDV disease. This research group is also optimizing dosing and timing of a promising MARV vaccine. Likewise, an experimental MARV vaccine candidate developed at the NIAID Vaccine Research Center (VRC) was recently evaluated in a Phase 1 study. This vaccine, known as cAd3-Marburg, induced strong, long-lasting immunity, with 95 percent of participants in the trial exhibiting a robust antibody response after vaccination and 70 percent maintaining that response for more than 48 weeks. A similar vaccine strategy against SUDV showed equally promising results in early clinical trials.

Bacteria can develop resistance to antimicrobial drugs, sometimes making them difficult or impossible to treat. NIAID continues to make advances in research on antimicrobial resistance (AMR) with support of the government-wide National Action Plan for Combatting Antibiotic-Resistant Bacteria and the Antibacterial Resistance Leadership Group (ARLG), a global consortium leading a comprehensive clinical research agenda. AMR is particularly problematic in some high-risk settings, such as in health care facilities, low-resource locations, and in populations with chronic medical conditions. For example, AMR bacteria are commonly found in the airways of people with cystic fibrosis (CF) and can lead to patient death. In a clinical trial launched in FY 2023, adults with CF were given bacteriophage, or "phage," therapy – viruses that directly infect and destroy bacteria, bypassing bacterial antibiotic resistance mechanisms. This trial, conducted by ARLG scientists, is evaluating whether phage therapy is safe and reduces the amount of antibiotic-resistant *Pseudomonas aeruginosa* bacteria in patients' lungs. Another NIAID-supported study is examining how *Staphylococcus aureus* (*S. aureus)* bacteria colonize the human body. A clinical trial found an orally-delivered probiotic, *Bacillus subtilis*, eliminated more than 95 percent of *S. aureus* bacteria in volunteers' bodies without altering the existing community of non-harmful microorganisms in the body, known as the microbiome. This research holds potential for controlling severe *S. aureus* infections common in high-risk settings. NIAID also is supporting innovative research that pursues vaccine development for *Clostridioides difficile* infection, the leading cause of antibiotic-associated diarrhea, and for

Universal Influenza Vaccines

Seasonal influenza, or flu, continues to kill thousands of people in the U.S. each year. Although current flu vaccines limit severity of influenza, they do not work against every flu strain and must be taken on an annual basis. An effective universal flu vaccine could protect against a wide variety of strains and provide durable long-term immunity, eliminating the need for people to get a flu shot yearly.

Flu vaccines teach the immune system to recognize and respond to a protein found on the surface of the influenza virus, called hemagglutinin (HA). The head of the HA protein can vary year to year and within strains, but the stem of the HA protein is similar across many different strains. NIAID researchers are developing vaccines to target this more consistent stem portion of the HA protein to induce long-term immunity against a broad range of flu viruses. A clinical trial of one such vaccine, H1ssF (influenza H1 hemagglutinin stabilized stem ferritin nanoparticle vaccine), showed it was safe, well-tolerated, and induced broad antibody responses. Based on these positive results, NIAID recently began a separate clinical trial of an H1ssF vaccine – this time using a mRNA delivery system – to test its safety and ability to induce an appropriate immune response. NIAID also is conducting a Phase 1 clinical trial of FluMos-v2, designed to provide long-lasting protection against multiple flu virus strains by displaying part of six different HA proteins on self-assembling nanoparticle scaffolds.

Using a different vaccine approach, NIAID recently completed a Phase 1 clinical trial for a vaccine candidate, BPL-1357, a whole-virus vaccine made up of four strains of non-infectious, chemically inactivated, low-pathogenicity avian flu virus. This vaccine was administered intramuscularly or intranasally to assess the importance of mucosal immunity against flu. By developing and testing multiple platform and antigen combinations for a universal flu vaccine, researchers increase the chances that they find one that is both safe and provides strong and broad immunity against a variety of strains.

preclinical development of MCMs against AMR bacteria and fungi that are significant threats to public health.

Mosquitoes and ticks are the most important vectors of pathogens causing human diseases such as malaria, dengue fever, Zika, and Lyme. NIAID supports research to better understand and respond to these pathogens. Recently, an NIAID-supported study identified a highly potent neutralizing antibody against Zika with potential to be a safe and effective treatment, particularly during pregnancy, where individuals experience the most severe consequence of the disease. Some mosquito- and tick-borne viruses pose unique challenges to vaccine design due to their complex interactions with the immune system. An NIAID-sponsored clinical trial of a new dengue vaccine, DENV3, is assessing whether side effects and immune responses are different depending on a person's previous exposure to dengue virus. Additionally, NIAID scientists and colleagues are working to develop safe and effective therapies with broad protection against multiple alphaviruses, including Venezuelan equine encephalitis virus and chikungunya virus. Alphaviruses are spread primarily by mosquitos and can cause disease that can manifest as severe neurological disease or crippling muscle pain. A monoclonal antibody, SKT05, that targets multiple alphaviruses provided protection from both manifestations of disease in animal studies. NIAID is also supporting research to better understand Post-Treatment Lyme Disease Syndrome (PTLDS), a collection of symptoms that linger following standard treatment for Lyme disease. The bacterium that causes Lyme disease, *Borrelia burgdorferi*, is spread by the blacklegged tick, *Ixodes scapularis*.

As part of its dual mandate, NIAID maintains readiness to respond to disease threats when they emerge or re-emerge. As part of its ongoing preparedness efforts, NIAID is funding a new Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness (ReVAMPP) Network. The goal of this network is to develop vaccine and monoclonal antibody strategies for representative viruses from families of pandemic concern. Another NIAID

preparedness program, the Centers for Research in Emerging Infectious Diseases (CREID) Network, brings together multidisciplinary teams to conduct integrated research for detecting, controlling, and preventing emergence or re-emergence of viral infectious diseases. The CREID network focuses on surveillance studies to identify previously unknown viral causes of febrile illnesses in humans, including the animal sources of, and genetic changes within, these pathogens that allow them to infect humans. At the NIAID VRC, the Pandemic REsponse REpository through Microbial and Immune Surveillance and Epidemiology (PREMISE) program uses both pathogen surveillance and immunological surveillance to develop stockpiles of immunobiological MCMs. The Antiviral Drug Discovery (AViDD) Centers conduct innovative, multidisciplinary research to develop drugs targeting specific viral families with high potential to cause a future pandemic. AViDD is a part of the Antiviral Program for Pandemics (APP), which awarded contracts in FY 2023 to develop antivirals for filoviruses (e.g., Ebola), chikungunya virus, and yellow fever virus.

Budget Policy:
The FY 2025 President's Budget request for the extramural component of Biodefense and Emerging Infectious Diseases research supported by NIAID is $2,199.9 million, which is a decrease of $9.9 million from the FY 2023 Final level. NIAID will continue to conduct and support research to better understand, prevent, and treat infectious diseases of public health concern.

The FY 2025 request will support the development of MCMs for SARS-CoV-2 and new platform technologies as part of a strategy to address emerging and re-emerging infectious disease pathogens. This budget includes funding 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 and immune-mediated diseases, many of which have far-reaching global consequences. These diseases include malaria, neglected tropical diseases, hepatitis, sexually transmitted infections (STIs, including genital herpes, gonorrhea, and syphilis), fungal diseases, autoimmune diseases, asthma, and allergic diseases. In addition, NIAID conducts research to improve the long-term success of organ, tissue, and cell transplantation by better understanding the role the immune system plays in transplant success or failure.

Allergic diseases and asthma affect more than 20 percent of the U.S. population and disproportionally impact various racial, ethnic, and socioeconomic groups. NIAID is funding studies to compare the presentation, causes, course, and management of food allergy in children of diverse racial and ethnic backgrounds. NIAID also continues its long history of research on the causes and management of asthma in children living in low-income, urban communities. A recent study identified a strong relationship between airway pollution and asthma exacerbations in these children in the absence of a respiratory viral infection. In its efforts to understand the early causes of asthma in the U.S., an NIAID-funded birth cohort study has determined that 15 percent of cases of asthma at age 5 may be preventable if infection due to respiratory

syncytial virus (RSV) in the first year of life is avoided. Eczema is often unpredictable, and symptoms can worsen from exposure to multiple substances or without any obvious trigger. NIAID scientists recently compared a database that collects information from clinic visits for eczema with two resources from the Environmental Protection Agency that track environmental exposures and found a previously undiscovered association between eczema and diisocyanates and xylene, chemicals found in clothing, to treat furniture, and in building materials. These studies highlight the need to comprehensively assess environmental exposures and sociodemographic factors that may impact risk of allergic conditions.

Celiac disease is an autoimmune disease that affects the gastrointestinal tract and occurs in genetically susceptible individuals who develop an immune response after ingesting gluten. Although the disease affects slightly over one percent of the U.S. population, the incidence has been rising over the last few decades. NIAID is supporting a NIH-wide funding opportunity, "Accelerating Progress in Celiac Disease Research," that will fund research to define the cause and pathogenesis of celiac disease, as well as projects to identify and develop strategies for celiac disease prevention and treatment.

Gut health also can impact other inflammatory conditions, including asthma, allergy, and autoimmune diseases. NIAID-funded researchers discovered that ILC2s cells, immune cells found in multiple tissues, are essential for protecting the gastrointestinal tract from parasitic infections but have also been associated with inflammation in allergy and asthma. Understanding the beneficial activities of ILC2s, as well as their undesirable roles in development of inflammatory diseases, is a critical new area of future research. Separately funded research identified a novel species of gut bacteria that may be involved in some cases of rheumatoid arthritis (RA), where the immune system attacks joints. While it has long been hypothesized that there is an association between bacteria and autoimmune disease, this study is among the first to demonstrate a strong connection between a specific bacterial species and development of RA.[2]

Malaria continues to be a significant global health burden. Approximately 247 million cases of malaria occurred worldwide in 2021, resulting in an estimated 619,000 deaths, mostly in children in sub-Saharan Africa.[3] Until recently, only one malaria vaccine (RTS,S) was recommended by the WHO. In October, WHO recommended a new vaccine, R21/Matrix-M, for the prevention of malaria in children. Nevertheless, WHO has called for further development of highly safe and efficacious malaria vaccines to reduce mortality and community-level transmission. NIAID-funded researchers tested a three-dose regimen of a whole-parasite vaccine, the Plasmodium falciparum sporozoite (PfSPZ) vaccine, and showed it was safe and effective in adults who have previously experienced malaria. NIAID also is studying how monoclonal antibodies may protect against malaria infection. An NIAID clinical trial showed that a single intravenous (IV) infusion of the antibody CIS43LS provided up to 88.2 percent efficacy against malaria infection over a 6-month malaria season in Mali. Another NIAID study identified, isolated, and modified a naturally occurring antibody to extend the length of time it could remain in the bloodstream. This antimalarial monoclonal antibody, L9LS, was still highly effective when give as an injection rather through IV administration. Phase 2 trials for L9LS are underway in Africa.

[2] ncbi.nlm.nih.gov/pmc/articles/PMC9804515/
[3] who.int/teams/global-malaria-programme/reports/world-malaria-report-2022

STIs have a devastating impact on long-term health, particularly when left untreated. The incidence of many STIs has been on the rise in the last decade in the U.S. and worldwide, and NIAID remains committed to addressing this lingering public health threat. One such threat, *Neisseria gonorrhoeae* (*N. gonorrhoeae*) – the causative agent of gonorrhea – is becoming resistant to most antibiotics. However, new Phase 3 clinical trial results show that a single dose of zoliflodacin, a novel, "first-in-class" oral antibiotic, is safe and effective as a treatment for gonorrhea. NIAID sponsored the Phase 1 and Phase 2 clinical trials that evaluated the safety and antimicrobial activity of zoliflodacin. These trials enabled the Phase 3 study, which was led by private sector partners. NIAID also recently funded research projects to study the clinical history (i.e., infection diagnosis through post-treatment follow-up) of syphilis, gonorrhea, and chlamydia to inform the development of vaccines and diagnostics for these STIs. Furthermore, NIAID plans to support efforts to develop vaccines for certain STI pathogens that have limited candidates in the product development pipeline: *N. gonorrhoeae* (gonorrhea), *Chlamydia trachomatis* (chlamydia), and *Treponema pallidum* (syphilis). In response to the persistent health challenges of herpes simplex virus 1 (HSV-1) and HSV-2, NIAID led the development of an NIH-wide Strategic Plan for Herpes Simplex Virus Research. The plan outlines an HSV research framework with four strategic priorities: improving fundamental knowledge of HSV biology, pathogenesis, and epidemiology; accelerating research to improve HSV diagnosis; improving strategies to treat HSV while seeking a curative therapeutic; and advancing research to prevent HSV infection.

Type 1 Diabetes Treatments

Type 1 diabetes (T1D) is a life-threatening autoimmune disease that requires individuals to take insulin for the rest of their lives to manage their blood sugar levels and reduce the risk of severe complications. The FDA approved two T1D therapies in the past year, both of which originated from long-standing NIAID-funded research efforts on T1D prevention and treatment.

In November 2022, after decades of NIH, academic, and industry investment in T1D prevention research, the FDA approved the first disease-modifying drug, teplizumab, to delay T1D. NIAID-funded investigators identified a human antibody, anti-CD3, that binds to T cells and prevents them from attacking beta cells, which produce insulin. Anti-CD3 was found to prevent T1D in mice but caused negative side effects in human patients, leading to studies to reengineer anti-CD3. The reengineered antibody, called teplizumab, was evaluated in two NIAID-supported clinical trials. It was shown to be safe and delayed progression of T1D in children.

In June 2023, the FDA approved Lantidra, the first Purified Human Pancreatic Islet (PHPI) therapy to treat individuals with T1D that is difficult to manage with conventional methods. Lantidra, licensed by CellTrans, is based on a PHPI product developed by the Clinical Islet Transplantation (CIT) consortium, a joint venture between NIAID and the National Institute of Diabetes and Digestive and Kidney Diseases. The CIT Consortium conducted the Phase 3 trial of PHPI, demonstrating its safety and efficacy in maintaining blood glucose levels and preventing severe low blood sugar events.

A recent WHO report on tuberculosis (TB) noted that the estimated numbers of new TB cases and deaths increased in 2021 for the first time in more than a decade.[4] *Mycobacterium tuberculosis*, the bacterium that causes TB, is highly contagious and transmitted in aerosolized droplets that are inhaled by a nearby individual. Recent NIAID research revealed that even

[4] who.int/news/item/14-10-2021-tuberculosis-deaths-rise-for-the-first-time-in-more-than-a-decade-due-to-the-covid-19-pandemic

normal breathing can aerosolize TB bacteria, suggesting that TB may be transmitted more readily than previously thought. NIAID is funding research on the primary drivers of TB transmission and is supporting the development of safe and effective TB vaccines. A recent Phase 1 trial found that a freeze-dried version of an experimental TB vaccine was safe and induced an immune response in healthy adults. This vaccine candidate has the advantage of being stable at room temperatures, making it easier to transport to remote parts of the world than conventional vaccines. Ongoing TB treatment efforts include Phase 1 clinical trials by the Gates Medical Research Institute on a new TB-selective antibacterial drug candidate that was developed jointly by NIAID and Merck scientists. The drug, designed to be taken once daily by mouth, likely will not cause the side effects triggered by a similar TB drug, linezolid. NIAID continues to support improvements in diagnosing TB, including support for the development of improved drug susceptibility tests, conducting the first evaluation of the Cepheid HR cartridge as a blood-based triage test, and supporting the development of diagnostic assays that use easy to obtain samples, including blood, urine, and oral swabs.

Organ transplantation is the treatment of choice for individuals with end-stage disease of the kidneys, heart, lungs, or liver. More than 100,000 Americans are currently on the transplant waiting list.[5] While organ transplantation extends and improves quality of life, it does not restore normal life expectancy: the immunosuppressive drugs currently required to protect the transplanted organ are associated with serious conditions including diabetes, cardiovascular disease, and kidney injury. NIAID aims to improve health and prolong survival in transplant recipients. To achieve this, NIAID supports basic and preclinical research and clinical trials that evaluate the role of the immune system in successful and failed organ transplants and develop approaches to selectively control or eliminate unwanted immune responses following transplantation. For example, NIAID-funded studies in NHPs have demonstrated the efficacy of novel B-cell directed therapies for the treatment of pre-sensitization, a condition in which individuals develop antibodies against proteins found on the surface of donor cells. This condition significantly interferes with the ability to find a compatible donor for a person with end-stage kidney disease. A therapy to prevent or treat pre-sensitization could improve outcomes for affected transplant recipients. These preclinical studies are the basis for recent NIAID-sponsored clinical trials intended to diminish pre-sensitization and enable more patients on the waiting list to receive a compatible organ. These studies are part of a broader portfolio evaluating novel interventions including cellular therapies and biologic agents for organ transplantation.

Budget Policy:
The FY 2025 President's Budget request for the extramural component of Infectious and Immunologic Diseases research is $1,543.8 million, which is an increase of $0.9 million from the FY 2023 Final level. NIAID will continue to advance long-range research priorities in infectious and immunologic diseases. The FY 2025 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.

[5] optn.transplant.hrsa.gov/data/

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 IRP has three components: 1) the Division of Intramural Research (DIR), with more than 124 principal investigators in Maryland and at the Rocky Mountain Laboratories in Montana who lead a wide range of basic, translational, and clinical research efforts in infectious diseases, allergy, and immunology; 2) the Vaccine Research Center (VRC), which applies fundamental advances in immunology, virology, and vaccine science to discover new and improved vaccines for human diseases; and 3) the Division of Clinical Research (DCR), which facilitates efficient and effective NIAID clinical research programs in the U.S. and internationally.

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. For example, NIAID scientists played key roles in the discovery and development of the first FDA-approved RSV vaccines for people aged 60 and older and pregnant individuals. NIAID scientists discovered that the RSV surface F protein induced a protective immune response and that the F protein altered its shape between two conformations, known as the prefusion and postfusion states. "Locking" the RSV F protein in its prefusion state induced a stronger immune response than the "unlocked" F protein. Beginning in 2017, NIAID VRC and other NIAID-funded scientists tested a vaccine using this "locked" prefusion F protein in early clinical trials and demonstrated that it was safe and induced a protective immune response. After further development and testing by private industry, the FDA approved two separate RSV vaccines in 2023, both based on the "locked" prefusion F immunogen. The IRP also developed an RSV vaccine candidate for children 6-24 months of age, who are at risk of severe respiratory illness from RSV. This intervention, which is a live-attenuated vaccine candidate delivered intranasally, was developed by DIR researchers and offers protection by inducing systemic and mucosal immunity in the respiratory tract. DIR investigators partnered with academic and industry partners to advance its development.

IRP investigators continue to advance research on diseases with broad public health impact, including those spread by vectors such as ticks and mosquitoes. For example, DIR researchers recently used an NHP model to evaluate a DNA plasmid-based vaccine candidate regimen targeting Crimean-Congo hemorrhagic fever virus (CCHFV), a tick-borne febrile illness that can progress to severe, hemorrhagic disease. The vaccine offered robust protection against CCHFV through antibody-dependent and antibody-independent mechanisms. DIR researchers also have made headway against the transmission of malaria, a devastating global health problem. Transmission-blocking vaccine candidates targeting the development of the *Plasmodium falciparum* parasite in the mosquito host have shown promise in pre-clinical studies. NIAID also plans to establish an intramural research program on vector-borne pathogens in Uganda that will include ecological studies, pathogen characterization, disease modeling in animals, and development of MCMs.

Budget Policy:
The FY 2025 President's Budget request for Intramural Research is $879.9 million, which is an increase of $23.6 million from the FY 2023 Final level. The FY 2025 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, RSV, 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. The budget increase will support the January 2024 pay increase as well as the proposed January 2025 pay increase for intramural staff.

Research Management and Support
RMS activities provide administrative, budgetary, logistical, and scientific support in the review, awarding, and monitoring of research grants, training awards, and research and development contracts. RMS also facilitates NIAID-wide coordination, evaluation of programs, and strategic planning, which is coordinated through the NIAID Policy, Planning, and Evaluation (PP&E) Branch. In September 2022, NIAID published the Strategic Plan for Research to Develop a Valley Fever Vaccine with three strategic priorities to advance Valley fever vaccine research. Led by NIAID, NIH published the Strategic Plan for Herpes Simplex Virus (HSV) Research in September 2023. RMS activities also provide regulatory compliance, international coordination, and liaison activities with other federal agencies, Congress, and the public.

Budget Policy:
The FY 2025 President's Budget request for RMS is $436.0 million, an increase of $17.3 million from the FY 2023 Final level. The budget increase will support mandatory increases in NIH assessments and personnel costs.

NATIONAL INSTITUTES OF HEALTH
National Institute of Allergy and Infectious Diseases

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	$5,062,279,000	$6,562,279,000	$6,562,279,000
Rescission				$0
2025	$6,581,291,000			

[1] Budget Estimate to Congress includes mandatory financing.

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Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2024 Amount Authorized	FY 2024 CR	2025 Amount Authorized	FY 2025 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$6,562,279,000	Indefinite	$6,581,291,000
National Institute of Allergy and Infectious Diseases	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$6,562,279,000		$6,581,291,000

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Amounts Available for Obligation [1]

(Dollars in Thousands)

Source of Funding	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
Appropriation	$6,562,279	$6,562,279	$6,581,291
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*($0)*	*($0)*	*($0)*
Other Mandatory financing	*($0)*	*($0)*	*($0)*
Subtotal, adjusted appropriation	$6,562,279	$6,562,279	$6,581,291
OAR HIV/AIDS Transfers	-$627	$0	$0
Subtotal, adjusted budget authority	$6,561,652	$6,562,279	$6,581,291
Unobligated balance, start of year	$0	$0	$0
Unobligated balance, end of year (carryover)	$0	$0	$0
Subtotal, adjusted budget authority	**$6,561,652**	**$6,562,279**	**$6,581,291**
Unobligated balance lapsing	-$110	$0	$0
Total obligations	$6,561,542	$6,562,279	$6,581,291

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:
FY 2023 - $36,425 FY 2024 - $40,000 FY 2025 - $40,000

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

		FY 2024 CR	FY 2025 President's Budget
Total compensable workyears:			
	Full-time equivalent	2,180	2,180
	Full-time equivalent of overtime and holiday hours	0	0
	Average ES salary	$223	$229
	Average GM/GS grade	12.7	12.7
	Average GM/GS salary	$136	$140
	Average salary, Commissioned Corps (42 U.S.C. 207)	$118	$121
	Average salary of ungraded positions	$175	$179
	OBJECT CLASSES	**FY 2024 CR**	**FY 2025 President's Budget**
	Personnel Compensation		
11.1	Full-Time Permanent	$218,498	$224,616
11.3	Other Than Full-Time Permanent	$90,877	$93,421
11.5	Other Personnel Compensation	$15,498	$15,932
11.7	Military Personnel	$4,576	$4,790
11.8	Special Personnel Services Payments	$29,958	$30,797
11.9	**Subtotal Personnel Compensation**	**$359,408**	**$369,557**
12.1	Civilian Personnel Benefits	$120,315	$124,343
12.2	Military Personnel Benefits	$1,083	$1,134
13.0	Benefits to Former Personnel	$0	$0
	Subtotal Pay Costs	**$480,806**	**$495,034**
21.0	Travel & Transportation of Persons	$7,152	$7,331
22.0	Transportation of Things	$1,921	$1,995
23.1	Rental Payments to GSA	$82	$84
23.2	Rental Payments to Others	$2	$2
23.3	Communications, Utilities & Misc. Charges	$2,119	$2,117
24.0	Printing & Reproduction	$10	$10
25.1	Consulting Services	$228,683	$231,404
25.2	Other Services	$183,378	$176,365
25.3	Purchase of Goods and Services from Government Accounts	$685,281	$674,419
25.4	Operation & Maintenance of Facilities	$10,243	$10,400
25.5	R&D Contracts	$840,883	$805,840
25.6	Medical Care	$6,362	$6,740
25.7	Operation & Maintenance of Equipment	$35,678	$36,317
25.8	Subsistence & Support of Persons	$0	$0
25.0	**Subtotal Other Contractual Services**	**$1,990,508**	**$1,941,485**
26.0	Supplies & Materials	$63,938	$66,525
31.0	Equipment	$23,724	$24,473
32.0	Land and Structures	$5,353	$5,471
33.0	Investments & Loans	$0	$0
41.0	Grants, Subsidies & Contributions	$3,985,952	$4,036,052
42.0	Insurance Claims & Indemnities	$0	$0
43.0	Interest & Dividends	$712	$712
44.0	Refunds	$0	$0
	Subtotal Non-Pay Costs	**$6,081,473**	**$6,086,257**
	Total Budget Authority by Object Class	**$6,562,279**	**$6,581,291**

[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 2024 CR	FY 2025 President's Budget
Personnel Compensation		
Full-Time Permanent (11.1)	$218,498	$224,616
Other Than Full-Time Permanent (11.3)	$90,877	$93,421
Other Personnel Compensation (11.5)	$15,498	$15,932
Military Personnel (11.7)	$4,576	$4,790
Special Personnel Services Payments (11.8)	$29,958	$30,797
Subtotal, Personnel Compensation (11.9)	**$359,408**	**$369,557**
Civilian Personnel Benefits (12.1)	$120,315	$124,343
Military Personnel Benefits (12.2)	$1,083	$1,134
Benefits to Former Personnel (13.0)	$0	$0
Subtotal Pay Costs	**$480,806**	**$495,034**
Travel & Transportation of Persons (21.0)	$7,152	$7,331
Transportation of Things (22.0)	$1,921	$1,995
Rental Payments to Others (23.2)	$2	$2
Communications, Utilities & Misc. Charges (23.3)	$2,119	$2,117
Printing & Reproduction (24.0)	$10	$10
Other Contractual Services		
Consultant Services (25.1)	$228,683	$231,404
Other Services (25.2)	$183,378	$176,365
Purchase of Goods and Services from Government Accounts (25.3)	$521,224	$509,887
Operation & Maintenance of Facilities (25.4)	$10,243	$10,400
Operation & Maintenance of Equipment (25.7)	$35,678	$36,317
Subsistence & Support of Persons (25.8)	$0	$0
Subtotal Other Contractual Services	**$979,205**	**$964,373**
Supplies & Materials (26.0)	$63,938	$66,525
Subtotal Non-Pay Costs	**$1,054,347**	**$1,042,352**
Total Administrative Costs	**$1,535,153**	**$1,537,386**

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Detail of Full-Time Equivalent Employment (FTE)

Office	FY 2023 Final			FY 2024 CR			FY 2025 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Clinical Research									
Direct:	92	4	96	96	4	100	96	4	100
Total:	92	4	96	96	4	100	96	4	100
Division of Extramural Activities									
Direct:	256	2	258	262	2	264	262	2	264
Total:	256	2	258	262	2	264	262	2	264
Division of Intramural Research									
Direct:	746	7	753	766	7	773	766	7	773
Total:	746	7	753	766	7	773	766	7	773
Office of the Director									
Direct:	427	-	427	447	-	447	447	-	447
Total:	427	-	427	447	-	447	447	-	447
Division of Allergy, Immunology, and Transplantation									
Direct:	98	1	99	101	1	102	101	1	102
Total:	98	1	99	101	1	102	101	1	102
Division of Microbiology and Infectious Diseases									
Direct:	188	8	196	198	8	206	198	8	206
Total:	188	8	196	198	8	206	198	8	206
Division of Acquired Immunodeficiency									
Direct:	162	4	166	166	4	170	166	4	170
Total:	162	4	166	166	4	170	166	4	170
Vaccine Research Center									
Direct:	113	1	114	117	1	118	117	1	118
Total:	113	1	114	117	1	118	117	1	118
Total	2,082	27	2,109	2,153	27	2,180	2,153	27	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
2021	12.6
2022	12.7
2023	12.6
2024	12.7
2025	12.7

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Detail of Positions [1]

GRADE	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	$424,200	$445,622	$458,100
General Schedule			
GM/GS-15	213	231	231
GM/GS-14	434	447	447
GM/GS-13	422	438	438
GS-12	256	266	266
GS-11	132	141	141
GS-10	1	5	7
GS-9	62	65	67
GS-8	25	27	29
GS-7	50	52	56
GS-6	12	12	12
GS-5	4	5	6
GS-4	4	5	6
GS-3	3	3	3
GS-2	1	1	1
GS-1	4	4	4
Subtotal	1,623	1,702	1,714
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	7	8	9
Senior Grade	6	7	8
Full Grade	8	8	9
Senior Assistant Grade	3	4	4
Assistant Grade	0	0	0
Junior Assistant	0	0	0
Subtotal	24	27	30
Ungraded	501	509	509
Total permanent positions	1,628	1,639	1,650
Total positions, end of year	2,150	2,240	2,255
Total full-time equivalent (FTE) employment, end of year	2,109	2,180	2,180
Average ES salary	$212,100	$222,811	$229,050
Average GM/GS grade	12.6	12.7	12.7
Average GM/GS salary	$129,755	$136,308	$140,125

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