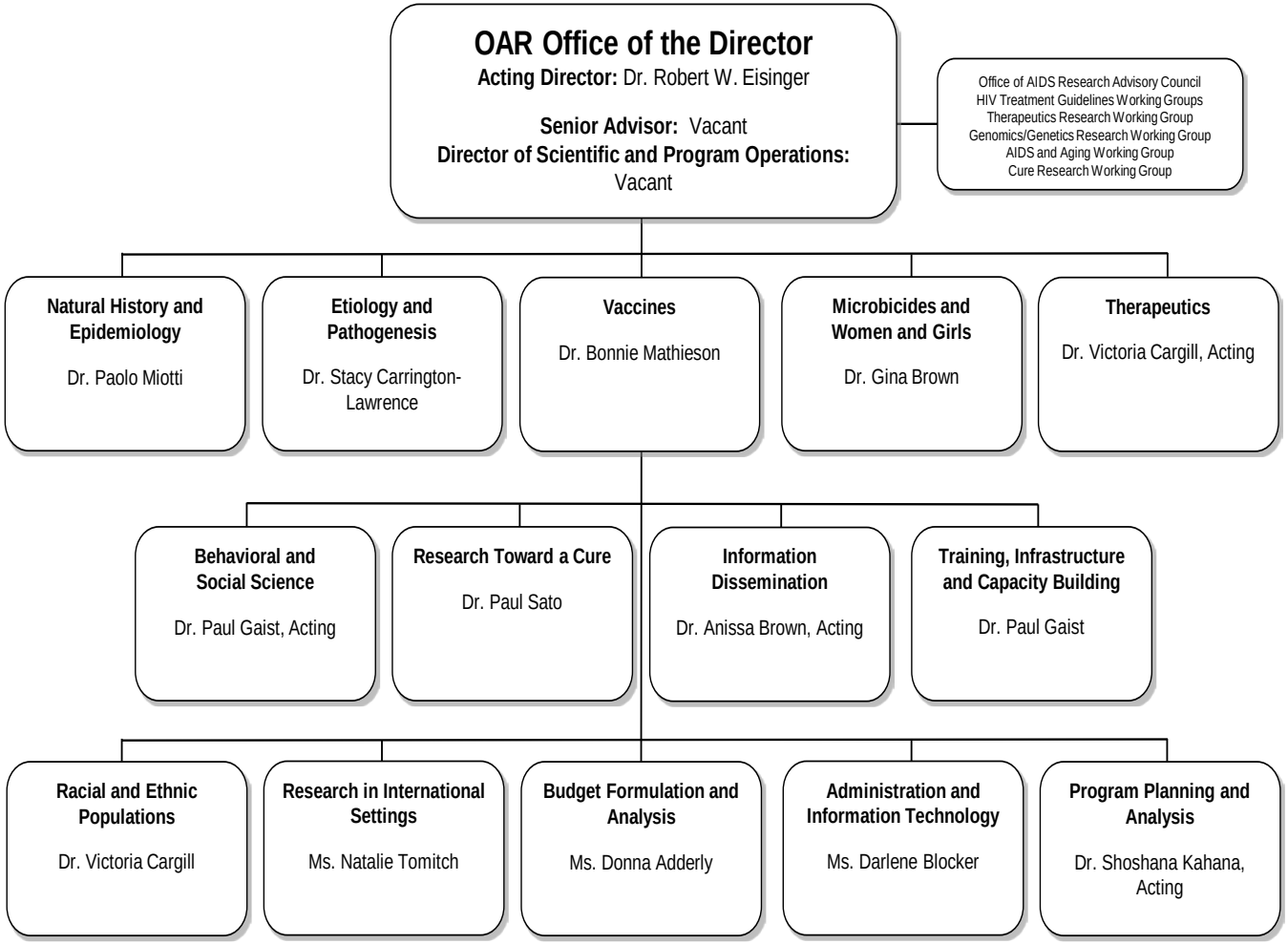
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Trans-NIH AIDS Research Budget

NOTE: The FY 2016 Enacted funding amounts cited throughout this chapter reflect the effects of OAR HIV/AIDS Transfers.


OAR Office of the Director
Acting Director: Dr. Robert W. Eisinger
Senior Advisor: Vacant
Director of Scientific and Program Operations: Vacant
Office of AIDS Research Advisory Council
HIV Treatment Guidelines Working Groups
Therapeutics Research Working Group
Genomics/Genetics Research Working Group
AIDS and Aging Working Group
Cure Research Working Group
Natural History and Epidemiology
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Etiology and Pathogenesis
Dr. Stacy Carrington-Lawrence
Vaccines
Dr. Bonnie Mathieson
Microbicides and Women and Girls
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Therapeutics
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Behavioral and Social Science
Dr. Paul Gaist, Acting
Research Toward a Cure
Dr. Paul Sato
Information Dissemination
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Training, Infrastructure and Capacity Building
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Research in International Settings
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Ms. Donna Adderly
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Ms. Darlene Blocker
Program Planning and Analysis
Dr. Shoshana Kahana, Acting

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Institute and Center
(Dollars in Thousands)

Institute / Center	FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget	FY 2017 +/- FY 2016
NCI	$269,660	$266,422	$266,422	$0
NHLBI	64,974	67,020	67,020	0
NIDCR	17,465	18,015	18,015	0
NIDDK	30,031	29,471	29,471	0
NINDS	45,465	46,536	46,536	0
NIAID	1,586,804	1,663,823	1,663,823	0
NIGMS	64,963	53,194	53,194	0
NICHD	142,016	144,736	144,736	0
NEI	1,360	925	925	0
NIEHS	5,179	5,342	5,342	0
NIA	5,465	5,637	5,637	0
NIAMS	4,779	4,587	4,587	0
NIDCD	1,821	1,878	1,878	0
NIMH	156,687	161,289	161,289	0
NIDA	298,862	294,244	294,244	0
NIAAA	27,537	28,404	28,404	0
NINR	12,266	12,180	12,180	0
NHGRI	6,380	1,531	1,531	0
NIBIB	713	395	395	0
NIMHD	21,839	21,674	21,674	0
NCCIH	975	777	777	0
NCATS	64,287	0	0	0
FIC	23,520	24,083	24,083	0
NLM	7,937	8,822	8,822	0
OD				
OAR	61,923	62,256	62,256	0
ORIP	77,153	76,820	76,820	0
Subtotal, OD	139,076	139,076	139,076	0
TOTAL, NIH	**$3,000,061**	**$3,000,061**	**$3,000,061**	**$0**

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS [1]

(Dollars in Thousands)

MECHANISM	FY 2015 Actual		FY 2016 Enacted		FY 2017 President's Budget		FY 2017 +/- FY 2016	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,643	$1,241,614	1,679	$1,311,454	1,698	$1,390,186	19	$78,732
Administrative Supplements	*(82)*	9,798	*(45)*	7,039	*(47)*	7,139	*(2)*	100
Competing	634	374,740	587	376,337	491	305,823	-96	-70,514
Subtotal, RPGs	2,277	$1,626,152	2,266	$1,694,830	2,189	$1,703,148	-77	$8,318
SBIR/STTR	62	33,237	62	31,381	68	29,018	6	-2,363
Research Project Grants	2,339	$1,659,389	2,328	$1,726,211	2,257	$1,732,166	-71	$5,955
Research Centers:								
Specialized/Comprehensive	180	$131,550	172	$123,086	169	$119,240	-3	-$3,846
Clinical Research	1	59,553	0	0	0	0	--	--
Biotechnology	0	240	0	246	0	246	--	--
Comparative Medicine	18	61,460	29	61,769	29	61,769	--	--
Research Centers in Minority Institutions	12	6,396	9	5,279	7	2,897	-2	-2,382
Research Centers	211	$259,199	210	$190,380	205	$184,152	-5	-$6,228
Other Research:								
Research Careers	257	$42,510	261	$41,702	246	$44,245	-15	$2,543
Cancer Education	0	0	0	0	0	0	--	--
Cooperative Clinical Research	5	11,382	5	11,382	5	11,382	--	--
Biomedical Research Support	1	1,989	1	1,644	1	1,644	--	--
Minority Biomedical Research Support	1	375	1	375	1	375	--	--
Other	164	58,029	174	64,233	175	61,674	1	-2,559
Other Research	428	$114,285	442	$119,336	428	$119,320	-14	-$16
Total Research Grants	2,978	$2,032,873	2,980	$2,035,927	2,890	$2,035,638	-90	-$289
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	114	$4,661	104	$4,874	101	$4,769	-3	-$105
Institutional Awards	618	32,915	298	16,083	296	15,875	-2	-208
Total Research Training	732	$37,576	402	$20,957	397	$20,644	-5	-$313
Research & Develop. Contracts	94	$395,597	98	$399,991	100	$401,065	2	$1,074
(SBIR/STTR) (non-add)	*(6)*	*(2,707)*	*(9)*	*(5,197)*	*(9)*	*(5,197)*	--	--
Intramural Research		$346,998		$352,115		$351,545		-$570
Res. Management and Support		125,094		128,815		128,913		98
Res. Management & Support (SBIR Admin) (non-add)								
Office of the Director - Appropriation		*139,076*		*139,076*		*139,076*		--
Office of the Director - Other [2]		61,923		62,256		62,256		--
ORIP (non-add) [2]		*77,153*		*76,820*		*76,820*		--
Total, NIH Discretionary B.A.		**$3,000,061**		**$3,000,061**		**$3,000,061**		**$0**

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

[2] Number of grants and dollars for the ORIP components of OD are distributed by mechanism and are noted here as a non-add.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Activity
(Dollars in Thousands)

Area of Emphasis	FY 2013 Actual	FY 2014 Actual	FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget	FY 2017 +/- FY 2016
Vaccines	$518,170	$532,671	$534,987	$552,803	$553,910	$1,107
HIV Microbicides	111,240	107,843	106,104	109,656	108,881	(775)
Behavioral and Social Science	397,377	411,723	411,359	421,669	421,395	(274)
Etiology and Pathogenesis	625,027	666,569	597,518	602,180	599,106	(3,074)
Therapeutics						
Therapeutics as Prevention	*69,375*	*75,638*	*71,698*	*79,775*	*78,617*	*-1,158*
Drug Discovery, Development, and Treatment	*632,123*	*660,194*	*595,543*	*570,534*	*566,670*	*(3,864)*
Total, Therapeutics	701,498	735,832	667,241	650,309	645,287	(5,022)
Toward a Cure [1/]	-	-	161,045	187,280	198,723	11,443
Natural History and Epidemiology	243,454	228,830	232,078	237,440	237,630	190
Training, Infrastructure, and Capacity Building	261,921	259,866	249,376	199,973	196,855	(3,118)
Information Dissemination	39,178	34,245	40,353	38,751	38,274	(477)
Total	$2,897,865	$2,977,579	$3,000,061	$3,000,061	$3,000,061	$0

[1/] **Beginning in FY 2017, Toward a Cure will be a separate activity. Dollars for Toward a Cure were previously included within other science areas, such as Therapeutics, Etiology and Pathogenesis, and Vaccines. The FY 2015 and FY 2016 amounts are comparable budget figures.**

NATIONAL INSTITUTES OF HEALTH

The AIDS Epidemic

(Dollars in Thousands)

According to the latest UNAIDS statistics reported in 2015 (in summary):

- 15.8 million people accessing antiretroviral therapy
- 36.9 million [34.3 million–41.4 million] people globally were living with HIV
- 2 million [1.9 million–2.2 million] people became newly infected with HIV
- 1.2 million [980,000–1.6 million] people died from AIDS-related illnesses
- TB-related deaths in people living with HIV have fallen by 32% since 2004. However, TB remains the leading cause of death among people living with HIV.
- 73% [68%-79%] of pregnant women living with HIV had access to antiretroviral medicines to prevent transmission of HIV to their babies in 2014; new HIV infections among children were reduced by 58% from 2000 to 2014.

According to the latest CDC statistics reported in 2015 (in summary):

- Roughly 1.2 million people in the U.S. were living with HIV
- Approximately 40,000 new HIV infections diagnosed each year
- From 2005-2014, the annual number of HIV diagnoses in the U.S. declined 19% – driven by substantial declines among heterosexuals (down 35%) and people who inject drugs (down 63%).
- **Among women**- African American women have achieved the largest decreases, with a 42% decline since 2005 and a 25% decline in the most recent five-year period alone. Despite these recent gains, African American women continue to be disproportionately affected by HIV, accounting for 6 in 10 diagnoses among women in 2014. Diagnoses among Latino and white women have also declined steadily over the decade (35% and 30%, respectively).
- **Among men**- Gay, bisexual, and other MSM continue to be the group most heavily affected by HIV in the U.S. MSM represent approximately 2% of the U.S. population, but they accounted for nearly 67% of all persons with HIV diagnosed in 2014. From 2005-2014, diagnoses among MSM overall increased by roughly 6% (25,155 to 26,612), driven by increases among black and Latino MSM.
- **Among racial and ethnic populations**- While African Americans represent approximately 13% of the total U.S. population, they accounted for almost half (44%) of all HIV diagnoses in 2014. Similarly, Latino men and women accounted for 23% of all new HIV diagnoses, while only representing 17% of the population.
- **Among the southern region**- Southern states bear the greatest burden of HIV infection, illness, and death. Southern states account for an estimated 44% of all people living with an HIV diagnosis, despite making up roughly one-third (37%) of the national population. In addition, people living with HIV in the South are less likely to be aware of their infection than those living in other U.S. regions.
- **Among individuals over 50**- In 2013, people aged 50 and over accounted for 21% (8,575) of an estimated 47,352 HIV diagnoses in the United States. Of these, the largest number (44%, 3,747) were among those aged 50 to 54.
- **Among youth**- An estimated 9,961 youth were diagnosed with HIV infection in the U.S. in 2013, representing 21% of an estimated 47,352 people diagnosed during that year. 81% of these diagnoses occurred in those aged 20 to 24, the highest number of HIV diagnoses of any age group.

Justification of Budget Request

Office of AIDS Research
Trans-NIH AIDS Research Budget Justification
(see also: OAR section in Office of the Director/DPCPSI)

Budget Authority (BA):

FY 2015 Actual	FY 2016 Enacted	FY 2017 President's Budget	FY 2017+/- FY 2016
$3,000,061,000	$3,000,061,000	$3,000,061,000	---

Acting Director's Overview

Groundbreaking Accomplishments with Unprecedented Scientific Opportunities: In more than three decades since the first cases of AIDS were reported, NIH has been the global leader in sponsoring research to prevent, diagnose, and treat HIV and its associated comorbidities, coinfections, and other complications. NIH has established a comprehensive and coordinated AIDS research program that has demonstrated unprecedented progress against this global AIDS epidemic. NIH-sponsored research has led to groundbreaking advances in understanding the HIV life cycle, development of safe and effective antiretroviral drugs and drug regimens for the treatment of HIV-infected individuals, and strategies to prevent HIV transmission/acquisition. While significant progress has been made, the AIDS pandemic continues to spread in the United States and worldwide representing the most serious global public health crisis of our time. NIH will continue to build on the scientific advances and knowledge that has been gained to address the unprecedented scientific opportunities that we now face to successfully develop a safe and effective AIDS vaccine, a cure for AIDS, and ultimately, lead to an AIDS-free generation and an end to the AIDS pandemic.

Coordinated Trans-NIH AIDS Research Program: The Trans-NIH AIDS research program that produced these critical accomplishments is coordinated and managed by the Office of AIDS Research (OAR), which functions as an "institute without walls" with responsibility for HIV/AIDS research supported by nearly every NIH IC. It is essential to point out that because HIV/AIDS affects virtually every organ system, with a myriad of HIV-associated co-infections, malignancies, co-morbidities and other clinical complications, NIH-sponsored HIV/AIDS research supports a comprehensive portfolio that also includes research on these related health conditions in the context of HIV disease, including tuberculosis, hepatitis C, and AIDS-defining and non-AIDS defining cancers, neurologic complications, metabolic abnormalities, and cardiovascular conditions. OAR coordinates the scientific, budgetary, and policy elements of this diverse trans-NIH research program. OAR has established comprehensive trans-NIH AIDS planning, budgeting, and portfolio analysis processes to identify the highest-priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively. OAR also identifies specific funding for emerging scientific opportunities and public health challenges that require focused attention; manages and

facilitates multi-Institute and trans-Institute activities to address those needs; fosters research by designating funds and supplements for pilot program areas; facilitates international AIDS research and training; and sponsors scientific agenda setting workshops to identify new cutting-edge initiatives.

Annual Trans-NIH Strategic Plan and Budget: OAR plans and coordinates this research through the development of an annual Trans-NIH Plan for HIV-Related Research (Strategic Plan) that identifies overarching HIV/AIDS research priorities and specific research objectives and strategies. This comprehensive and unique annual strategic planning process involves scientists from across NIH and other Federal agencies, non-government experts, and representatives from community constituency groups. OAR also is legislatively mandated to develop an annual Trans-NIH AIDS research budget explicitly tied to the Strategic Plan. OAR's AIDS research allocation to each NIH IC is not based on a formula, but on the overarching HIV/AIDS research priorities identified in the Notice in the *NIH Guide for Grants and Contracts* on August 12, 2015 (NOT-OD-15-137), taking into account the current and emerging scientific opportunities, the evolving clinical profile of the epidemic, and the Institutes and Centers capacity to absorb and expend resources for the most meritorious science. This process reduces redundancy, promotes harmonization, and ensures cross-Institute collaboration to conduct and support research in domestic and international settings.

Priority-Setting Review: The overarching priorities were developed based on the OAR Advisory Council HIV/AIDS Research Portfolio Review Working Group Report, the FY 2015 Trans-NIH Plan for HIV-Related Research, and NIH leadership input. The priorities are also aligned with the NIH Director's themes as indicated below.

- **Foundation for Discoveries - Basic Research**: NIH-sponsored basic research provides the critical foundation, tools, and building blocks for the development and testing of new and better strategies to prevent and treat HIV infection and AIDS. The focus on basic research will lead to the development of AIDS vaccine candidates, potential microbicides, approaches to achieving a cure for AIDS, and innovative HIV prevention interventions.
- **The Promise of Precision Medicine**: NIH will continue to support research leading to improved treatments for HIV disease that have fewer side effects and toxicities, easier adherence, and longer and sustained acting anti-HIV drugs. Research will focus on how sex, gender, race, age, genetic determinants, treatment during pregnancy, nutritional status, and other factors interact with anti-HIV treatment. Another key priority is the development of strategies to prevent and treat HIV-associated coinfections, including hepatitis C and tuberculosis, and comorbidities such as malignancies, neurologic, metabolic, cardiovascular, and other complications.
- **Applying Big Data and Technology to Improve Health:** NIH will provide support to expand the development and use of new research tools including geo-spatial mapping and geo-statistical analysis to better understand the spatio-temporal evaluation of the AIDS pandemic. These tools and techniques also will provide critical insight on monitoring and maximizing access to care and treatment, as well as delineate new HIV-associated comorbidities and adverse events associated with antiretroviral treatment.

- **Stewardship to Inspire Public Trust:** NIH is utilizing a unique portfolio review process to annually assess all grants, contracts, and intramural projects supported with AIDS funding. This new process ensures that precious AIDS resources are directed to the new overarching NIH HIV/AIDS research priorities.

OAR will continue to allocate and redirect resources across NIH ICs and across the key areas of science to address these priorities.

Challenges and Opportunities for FY 2017: The overarching priorities for NIH AIDS research reflected in this Trans-NIH AIDS research budget request are:

- **Reducing Incidence of HIV/AIDS** including: developing and testing promising vaccines, developing and testing microbicides and pre-exposure prophylaxis candidates and methods of delivery, especially those that mitigate adherence issues; and developing, testing, and implementing strategies to improve HIV testing and entry into prevention services.
- **Next generation of HIV therapies with better safety and ease of use** that are: developing and testing HIV treatments that are less toxic, longer acting, have fewer side effects and complications, and easier to take and adhere to than current regimens. Additionally, implementation research to ensure initiation of treatment as soon as diagnosis has been made, retention and engagement in these services, and achievement and maintenance of optimal prevention and treatment responses.
- **Research toward a cure** includes: developing novel approaches and strategies to identify and eliminate viral reservoirs that could lead toward a cure or lifelong remission of HIV infection, including studies of viral persistence, latency, reactivation, and eradication.
- **HIV-associated comorbidities, coinfections, and complications** that are: addressing the impact of HIV-associated comorbidities, including tuberculosis, malignancies, cardiovascular, neurological, and metabolic complications; and premature aging associated with long-term HIV disease and antiretroviral therapy.
- **Cross cutting areas**:
    - **Basic Research**: understanding the basic biology of HIV transmission and pathogenesis; immune dysfunction and chronic inflammation; host microbiome and genetic determinants; and other fundamental issues that underpin the development of high priority HIV prevention, cure, co-morbidities, and treatment strategies.
    - **Research to Reduce Health Disparities** in the incidence of new HIV infections or in treatment outcomes of those living with HIV/AIDS.
    - **Research Training** of the workforce required to conduct high-priority HIV/AIDS or HIV/AIDS-related research.

<u>Overall Budget Policy:</u>
To address these critical AIDS research priorities, the FY 2017 President's Budget estimate for the trans-NIH AIDS research program is $3,000.061 million, the same amount that was provided at the FY 2016 Enacted level. The OAR is authorized to allocate all dollars associated with this area of research across the NIH. Therefore, the total for AIDS research includes both extramural

and intramural research (including research management support, management fund, and service and supply fund); buildings and facilities; and training and evaluation. The total also includes basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the many HIV-associated malignancies, coinfections, comorbidities, and complications, including TB, hepatitis C, and HIV-associated cancers. Thus, the total for HIV/AIDS research is not comparable to spending reported for other individual diseases. This request provides funding to support high priority vaccine research as well as a significant increase in the area of research toward a cure to fulfill the final installment on the Presidential Initiative started in FY 2015, while maintaining the same level of funding as provided in FY 2016.

Program Descriptions and Accomplishments

Vaccines: The best long-term hope for controlling the AIDS pandemic is the development of safe, effective, and affordable AIDS vaccines that may be used in combination with other prevention strategies. NIH supports a broad AIDS vaccine research portfolio encompassing basic, preclinical, and clinical research, including studies to identify and better understand potentially protective immune responses in HIV-infected individuals and studies of improved animal models for the preclinical evaluation of vaccine candidates. New developments in HIV vaccine research have radically changed our thinking concerning the design of novel immunogens and strategies to employ them. Since the modest success of the RV144 trial in Thailand using a pox virus vector and HIV envelope protein boosts, NIH has supported unprecedented international collaborative investigations to identify how specific immune responses may protect against HIV acquisition. To build on the knowledge gained from these studies, clinical trials are ongoing to test the RV144 vaccine with different inserts to elicit specific protection in a high-risk population in South Africa. In parallel, an alternative adenovirus/poxvirus vectored vaccine with HIV protein boosts developed for global coverage of diverse HIV subtypes, will begin at sites in the United States and around the world. Discovery of new HIV envelope-specific broadly neutralizing antibodies (bnAbs) – capable of neutralizing multiple strains of HIV have been accelerated with the advent of new technologies for detection and isolation. New bnAbs have been extensively characterized, structurally mapped, and together, shown to bind to almost the entire surface of the HIV envelope. A new prevention study designated “AMP” will begin late 2015/early 2016 in the United States and Africa using one of these promising bnAbs, identified as VRC01. Results from this study will inform prophylactic vaccine trials as to the concentration of antibody required to prevent HIV acquisition. Promising pre-clinical vaccine candidates include a virus-vectored vaccine administered to rhesus macaques (rhesus cytomegalovirus, rhCMV) and designed to elicit only T cell immunity that successfully eradicated SIV in 50 percent of animals despite transient infection and viremia. In addition, an adenovirus poxvirus vector-based vaccine prime, protein boost strategy also showed 50 percent complete protection from SIV infection in non-human primates. Immune correlates associated with this vaccine candidate were predominately functional binding antibodies. These unprecedented results have led to exploration of new basic and translational immunological paradigms. While progress has been made, many knowledge gaps remain and additional studies are essential to build a safe and effective vaccine platform.

Budget Policy:
The FY 2017 President's Budget request for Vaccine research is $553.910 million, an increase of $1.107 million or 0.20 percent compared to the FY 2016 Enacted level. Resources will be directed toward the development and testing of improved vaccine candidates in additional clinical studies, both in the United States and abroad. NIH will provide additional resources for the development and production of several vaccine immunogens and further clinical trial site development. Innovative basic HIV vaccine research studies also will be supported to inform the development of new vaccine concepts that may induce higher levels of protective antibodies and prevent HIV infection more efficiently than vaccines already tested. Increased support will be provided for clinical trials that evaluate the ability of monoclonal antibodies from HIV-infected individuals to protect from acquisition, delay disease progression or eliminate HIV infected cells. In FY 2017, NIH will support development of improved animal models, including new models for critical vaccine challenge studies in non-human primates to test vaccine concepts and to inform testing of HIV vaccine candidates in clinical trials. NIH also will provide support for new initiatives to integrate systems biology with HIV vaccine discovery and the development of new approaches to measuring immune responses to HIV vaccine candidates that will more closely predict outcomes of parallel preclinical animal and human clinical studies. The increase provided to vaccine research reflect OAR's redirection of funds from other scientific areas to support critical research opportunities in this area.

HIV Microbicides: A safe and effective microbicide will be an important asset to the HIV prevention tool kit. Microbicides are compounds, including antiretroviral (ARV) drugs and other agents that could be applied topically or administered locally to prevent acquisition of HIV and other sexually transmitted infections. Microbicides could be used alone or in combination with other HIV prevention strategies. NIH supports a comprehensive and innovative microbicide research program that includes the screening, discovery, development, formulation, preclinical testing, and clinical evaluation of microbicide candidates. NIH supports basic research including studies in animal models aimed at understanding the mechanisms by which HIV crosses mucosal membranes and infects cells and innate and acquired immune modulation that facilitates or inhibits HIV acquisition. In addition, NIH supports behavioral and social science research on adherence to and the acceptability and use of, microbicides among various populations. These projects include the safety of microbicide use during pregnancy and menopause; studies in adolescents and in men who have sex with men; and implementation research to better understand how to integrate a potential microbicide into community prevention practices. Basic science and clinical studies have shown promise for the use of ARV-based microbicides as HIV prevention strategies. Studies are underway and being developed to test: different ARV- and non-ARV-based microbicide candidates; the safety of various microbicide formulations, including long-acting formulations; the safety and pharmacokinetics of microbicides combined with a contraceptive for multipurpose prevention; and microbicides combined with antimicrobial agents to simultaneously prevent HIV and other sexually transmitted infections. Microbicide formulations and new technologies that enhance adherence and do not require pericoital use also are being developed and studied. These include long-acting injectable microbicide candidates, long-acting subcutaneous potential microbicides, ARV and non-ARV containing nanofibers and nanoparticles for local application and injection, ARV-containing films, and intravaginal rings.

Budget Policy:
The FY 2017 President's Budget request for Microbicides research is $108.881 million, a slight decrease of $0.775 million or 0.71 percent compared to the FY 2016 Enacted level for this critical area of prevention research. In FY 2017, NIH will continue to support the development and evaluation of microbicide candidates including a robust pipeline of both ARV and non-ARV potential microbicides. NIH will support research needed for the development of criteria for the selection of candidate microbicides to be advanced through the different phases of preclinical and clinical studies including clinical safety and effectiveness studies, as well as behavioral and social science associated with adherence and acceptability of potential microbicides. NIH will continue to provide crucial support for the NIH-funded Microbicide Trials Network (MTN); basic research on mucosal changes of female and male adolescents during reproductive maturation; and innovative formulation strategies. OAR will continue to foster coordination and collaboration in microbicide research leading to the development and testing of novel microbicide candidates that can prevent HIV transmission and acquisition.

Behavioral and Social Science: Behavioral and Social Science research is an integral component of the overarching NIH HIV/AIDS research priorities. As studies continue to define a role for the use of antiretroviral therapy for HIV prevention, NIH continues to support a comprehensive behavioral and social sciences research program across the spectrum of HIV/AIDS prevention, treatment, care, and cure. This includes expanding its support of the behavioral and social sciences research to encompass research to understand how antiretroviral medications can best be used for prevention in specific populations and social contexts. Research findings continue to show a wide range of individual, interpersonal, social, structural, and other factors that contribute to and drive the AIDS pandemic. NIH-sponsored research has demonstrated that some HIV risk behaviors can be reduced in targeted populations through evidence-based interventions. NIH will continue to study approaches to change HIV risk behaviors and social contexts and to facilitate engagement and retention in HIV testing, prevention, and treatment services. NIH is supporting research to address factors associated with the HIV Care Continuum, and specifically on HIV care outcomes. Studies have highlighted that modifying these variables can promote reduced HIV risk and transmission, early access to medical care, reduce costs, extend life expectancy, and improve quality of life and well-being. NIH will continue to build on current, as well as develop new behavioral and social science research methods, tools, and study approaches including: data collection platform and survey design; module development; and experimentation grounded in behavioral and social science theory. These studies will increase our understanding of related behavioral and social processes; increase recruitment in clinical trials; enhance statistical analyses of behaviors, such as alcohol and illicit drug use, that can affect prevention and medication studies and outcomes; utilize the means to optimize ongoing research in view of emerging results; and identify behavioral issues relevant to genetic or genomic studies that are specifically HIV/AIDS focused. NIH also will continue to foster the integration of biomedical, behavioral, and social science strategies in clinical studies.

Budget Policy:
The FY 2017 President's Budget request for Behavioral and Social Science is $421.395 million, a slight decrease of $0.274 million or 0.06 percent compared to the FY 2016 Enacted level. NIH will continue to support initiatives integrating behavioral and social science strategies with

biomedical modalities. Research on the development of strategies to more effectively encourage HIV testing and engagement in preventive care and/or treatment for youth and racial and ethnic populations is a priority. Implementation science and comparative effectiveness research to: 1) ensure initiation of treatment as soon as diagnosis has been made; 2) engagement and retention in HIV care services; and 3) achievement and maintenance of optimal prevention and treatment responses (e.g., viral suppression) will be emphasized.

Etiology and Pathogenesis (Basic Science): NIH supports a comprehensive portfolio of basic research focused on the transmission, acquisition, establishment, and maintenance of HIV infection and the causes of HIV-associated immune deficiency and severe clinical complications. Research on basic HIV biology and HIV/AIDS pathogenesis has revolutionized the design of new drugs and treatment regimens, methodologies for diagnosis and tools for monitoring disease progression, and the safety and effectiveness of antiretroviral therapies. Ground-breaking strides have been made towards understanding the fundamental steps in the life-cycle of HIV, the host-virus interactions, and the clinical manifestations associated with HIV infection and AIDS. Additional research is needed to further the understanding of the virus and how it causes disease, including studies to delineate how sex, gender, age, ethnicity, race, pregnancy, nutritional status, and other factors interact to influence vulnerability to infection and disease progression; determine the role of immune dysfunction and chronic inflammation in HIV pathogenesis; and further the understanding of the development of HIV-associated co-morbidities, such as cardiovascular, neurological, metabolic, renal, and other clinical complications, malignancies, and co-infections. Research examining the host microbiome as well as the genetic determinants associated with HIV susceptibility, disease progression, and treatment response also is needed. These studies may lead to the development of customized therapeutic and preventive regimens formulated for an individual patient based on his or her genetics. NIH also prioritizes research examining the mechanisms by which HIV establishes and reactivates latent reservoirs of infection and studies that further the understanding of factors that are associated with the ability of the host to restrict HIV infection and/or mitigate HIV disease progression. A better understanding of these processes may help identify key targets for the development of new therapeutic, biomedical, and vaccine strategies to prevent or control HIV infection and possibly lead to a cure for HIV disease.

Budget Policy:
The FY 2017 President's Budget request for the basic research area of Etiology and Pathogenesis is $599.106 million, a decrease of $3.074 million or 0.51 percent compared to the FY 2016 Enacted level. NIH will support studies that elucidate the mechanisms responsible for the pathogenesis of comorbid conditions of various organ systems, including the contribution of the immune system, inflammation, and long-term ARV use on the development of these co-morbidities. In addition, studies that quantify the risk of acquiring HIV-associated coinfections, studying its mechanisms, and evaluating the interaction of co-infecting pathogens on HIV disease progression and vice versa will be supported. NIH will continue its support on HIV-associated comorbidities including AIDS-defining and non-AIDS defining malignancies, metabolic abnormalities, and Project REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV) that is evaluating the use of statin administration to reduce the risk for major adverse cardiovascular events in HIV-infected individuals.

Therapeutics

Drug Discovery, Development, and Treatment: Antiretroviral (ARV) treatment has resulted in profound immune recovery and enhanced immunologic and physiologic function in individuals who can consistently adhere to prescribed HIV treatment regimens and tolerate the associated occasional side effects and toxicities. Expansion of the classes of ARV drugs available has allowed for greater simplification of treatment regimens, thus enhancing adherence and increasing the potential for viral suppression. ARV treatment has not only delayed the progression of HIV infection to AIDS, it has been shown to be extremely effective at prolonging viral suppression, delaying the development of viral resistance, and reducing HIV-associated comorbidity and comortality. Recent data from the NIH-sponsored Strategies for Management of Anti-Retroviral Therapy, designated the SMART study, confirmed that ART significantly reduced the risk of HIV-associated opportunistic infections and all-cause mortality. Despite these treatment advances, many challenges remain including: 1) maintaining long-term treatment adherence to continue to suppress HIV replication which is critical to maintaining immune competence and prolonging the time to the development of drug resistance; 2) the ongoing morbidity and mortality associated with coinfections, such as hepatitis C, tuberculosis; 3) metabolic dysregulation associated with HIV infection; 4) AIDS-defining and non-AIDS defining cancers; 5) neurologic and other comorbidities associated with HIV disease and ART; and 6) the persistent disparities in HIV treatment outcomes across race, gender, and socioeconomic status. Hepatitis C remains a significant coinfection that affects the immunologic response to ARV therapy. Over the last several years, the development of the directly acting agents (DAA) has made it possible to achieve a virologic suppression in over 90 percent of treated individuals. Despite these advances in the treatment of HIV and hepatitis C coinfection, there remain many challenges including, but not limited to the impact of HIV disease on renal, endocrine, and metabolic functioning; the clearing of viral sanctuaries, and treating individuals with co-morbid mental health, substance abuse, and other conditions. NIH supports a comprehensive therapeutics research program to design, develop, and test drugs and drug regimens. Under development are new combinations of drugs and sustained release formulations and delivery systems to maintain an undetectable viral load, to overcome drug resistance and treatment failure, and to prevent and treat HIV-associated coinfections, comorbidities, and other complications. This program also supports pre-clinical trials of innovative strategies to eliminate viral reservoirs including testing therapeutic anti-HIV monoclonal antibodies with and without antiretroviral drugs. Building on the identification of the critical therapeutic interventions, NIH continues to support research on successful treatment of HIV disease.

Therapeutics as Prevention: A critical area of prevention research is the study of treatment strategies as a method to prevent new HIV infections. This approach builds on NIH-sponsored landmark clinical trials that demonstrated treatment of HIV-infected pregnant women could significantly reduce transmission of HIV from mother to child. Clinical results from a large NIH-sponsored international clinical trial, HIV Prevention Trials Network (HPTN) 052, showed that early initiation of ART in HIV-infected heterosexual individuals resulted in a 96 percent reduction in sexual transmission of HIV to their uninfected partner. Ongoing research continues to build on earlier groundbreaking studies that demonstrated the successful use of oral ARVs to prevent transmission of HIV in specific populations. The first landmark pre-exposure prophylaxis (PrEP) study, *iPrEx: Chemoprophylaxis for HIV Prevention in Men*, demonstrated

that a daily tablet containing a combination of two ARV drugs (Truvada-tenofovir/emtricitabine: medications that also are used as part of an HIV treatment regimen), can safely and effectively prevent HIV infection in some high-risk men who have sex with men (MSM) and transgender women who have sex with men. The study showed that uninfected participants who took a daily dose of Truvada experienced an average of 43.8 percent fewer HIV infections than those who received a placebo pill. Participants who adhered most closely to the daily drug regimen showed higher rates of effectiveness, up to 73 percent. Studies among two additional at-risk populations, women in heterosexual HIV serodiscordant couples and injection drug users, have shown PrEP to be effective in preventing HIV acquisition. These studies established the foundation for the clinical guidance supporting widespread use of PrEP to be effective in preventing HIV acquisition. These studies also served as the foundation for the clinical guidance supporting widespread use of PrEP and supported FDA approval for the use of Truvada as PrEP. NIH also is sponsoring additional studies to refine the opportunities and barriers to PrEP in special populations, including HPTN 073 that is studying PrEP in young Black MSM; HPTN 076 and HPTN 077 which are designed to determine the safety and acceptability of an injectable long-acting ARV (rilpivirine) and cabotegravir, respectively. NIH supports basic, translational, clinical, and implementation research to: develop combinations of antiretroviral drugs and compounds that can be used in sustained release formulations for potential new PrEP strategies; test PrEP in high-risk uninfected populations, including adolescents; evaluate post-exposure prophylaxis, the use of ARV to prevent infection after HIV exposure, including in a healthcare setting; develop improved regimens to prevent mother-to-child transmission; and evaluate a potential innovative prevention strategy known as "test and treat" to determine the impact of increased testing with immediate referral to treatment at the community level.

Budget Policy:
The FY 2017 President's Budget request for Therapeutics research is $645.287 million, a decrease of $5.022 million or 0.77 percent compared to the FY 2016 Enacted level. Funds will be provided to support high priority research on the development of novel anti-HIV therapies (based on identifying new drug targets), as well as the testing of new combinations of ARVs and sustained release formulations that are safe, support adherence, minimize side effects and toxicities, and result in durable suppression of viral activity. NIH will provide critical support for studies on 1) development of formulation strategies for long-acting and sustained release prevention products (e.g., PrEP); 2) nonpharmacological (or behavioral) therapies for ARV adherence; 3); development of new strategies to test and treat patients with HIV-related co-infections, including hepatitis C virus and tuberculosis; 4) conducting clinical studies on cardiovascular and other metabolic complications of HIV disease and ART; and 5) treatment of aging HIV-infected individuals to prevent transmission and reduce HIV-associated comorbidity and comortality.

Research Toward a Cure: While combination antiretroviral therapy (ART) has radically altered the course of HIV disease by improving health, prolonging life, and substantially reducing the risk of HIV transmission, research toward a cure for HIV/AIDS is an overarching priority for NIH. The need for lifelong ARV therapy carries with it a significant burden on HIV-infected individuals, social and family structures, and health care systems due to the risk of side effects and other clinical complications associated with ART. The experience of the "Berlin Patient," has demonstrated that sustained remission of HIV infection is possible. Subsequent

research suggests that an intervention inducing sustained HIV remission without ART that is safe, effective, and scalable could be an achievable near-term goal. Lifelong remission or viral eradication will be a more challenging long-term goal. Additional research is critically needed to better understand the mechanisms and dynamics of HIV persistence and latency in long-lived cells, much of it in hard to access tissue sites. Expansion of research on models of HIV infection in humans, including studies in nonhuman primates and small animals is critical. Research to identify robust biomarkers and assays that measure the size of the reservoir; predict viral rebound during an intensively monitored pause in ARV treatment; and/or are predictive of response to cure interventions are critically needed. Further advances in basic research and the development of novel cure interventions in the pipeline, including next generation monoclonal antibodies and/or their derivatives with improved killing of HIV-infected cells, and therapeutic vaccines, as well as other modalities that help enhance the ability of the immune system of HIV-infected individuals to suppress or kill HIV-infected cells, are also high priorities for NIH research toward a cure. Recent advances in this field have led to a better understanding of the cellular, tissue, and molecular biological underpinnings of HIV latency, persistence, and reservoir formation. Studies also have shown that only a small proportion of HIV provirus integrated into the genome of susceptible cells is replication competent, and thus limiting the capability of directing the production of complete virus particles, productively infecting other susceptible cells, and transmitting HIV to others. While a "gold standard" assay for measuring the replication-competent reservoir is critically needed, progress is being made in refining the current assay platforms in advancing this research. A NIH-sponsored small-scale clinical trial has recently demonstrated that the VRC01 broadly neutralizing antibodies can safely reduce HIV plasma viral load in HIV-infected individuals with a susceptible strain. These scientific advances provide the crucial foundation for continued progress in developing strategies to achieving a cure for HIV/AIDS.

Budget Policy:
The FY 2017 President's Budget request for Toward a Cure research is $198.723 million, an increase of $11.443 million or 6.11 percent compared to the FY 2016 Enacted level. As part of the President's Initiative on an HIV Cure, these funds will provide an expansion of programs targeting innovative approaches to control and eradicate HIV infection that may lead to a cure; identifying innovative approaches to quantify latent HIV reservoirs; and develop novel strategies for targeting viral reservoirs in the central nervous system without inducing reactivation. Research will continue to examine the mechanisms by which HIV establishes and reactivates latent reservoirs of infection as well as studies on the factors that are associated with the ability of the host to restrict HIV infection and/or mitigate HIV disease progression. A better understanding of these processes may help identify key targets for the development of new therapeutic and vaccine strategies to prevent or control HIV infection and possibly lead to a cure for HIV disease.

Natural History and Epidemiology: Natural history and epidemiologic research on HIV/AIDS is critical to monitoring epidemic trends, evaluation of prevention modalities, characterization of the clinical manifestations of HIV disease, and measurement of the effects of treatment regimens at the population level. Novel methodologies in the area of biostatistics, mathematical modeling, and laboratory technology have provided the basis for new epidemiological approaches in addressing HIV/AIDS. Geo-spatial methods (geo-mapping) and geo-statistical analysis are new

tools that epidemiological research currently utilizes to better understand the spatio-temporal evolution of the HIV epidemic as well as to maximize and monitor access to HIV treatment and care. Through these collaborations of multiple NIH ICs, multi-site epidemiologic studies in the United States have been characterizing new HIV-related comorbidities, identifying unexpected adverse effects resulting from diverse risk factors and/or treatment regimens and differentiating these occurrences from those directly related to HIV disease. These epidemiological studies also continue to provide the basis for generating new scientific hypotheses and are a necessary complement to experimental studies (randomized clinical trials) that establish the effectiveness of an intervention. As the AIDS epidemic continues to evolve, NIH will support carefully designed epidemiologic studies about the varied facets of the HIV epidemic and disease in domestic and international settings. NIH also will sponsor information technology for a broader access to and use of epidemiologic data and metadata. NIH currently supports a comprehensive research portfolio to study the epidemiologic characteristics of populations in which HIV is transmitted and the changing spectrum of HIV-related disease, including the occurrence of co-infections (e.g., tuberculosis, hepatitis C virus), malignancies, metabolic, cardiovascular, neurological, skeletal, and other complications. These studies have delineated the significant health disparities that are critical factors in the epidemic (e.g., racial and ethnic disparities in the United States; between industrialized and resource-constrained nations; between men and women; and health disparities based on sexual identity). Ongoing observational studies are adding focus on at-risk individuals from the rural South in the United States as well as the increasing proportion of individuals who are aging with HIV. Research on HIV-related health disparities and their impact on treatment access and effectiveness, as well as HIV prevention, is an NIH overarching HIV/AIDS research priority.

Budget Policy:
The FY 2017 President's Budget request for Natural History and Epidemiology is $237.630 million, a slight increase of $0.190 million or 0.08 percent compared to the FY 2016 Enacted level. NIH will continue to support and prioritize research to better define networks of HIV transmission among demographic groups at highest risk for HIV infection in the United States, including men who have sex with men (MSM), especially MSM of color, and African American women. In addition, NIH will support research to better understand the physiological aspects of co-infection of sexually transmitted infections and HIV and how that relates to HIV transmission among at risk populations. Population studies on the long-term effects of HIV disease and ART will continue to be supported as will research that capitalizes on "big data" (existing data resources) and the use of sophisticated computational modeling to identify patterns of HIV and its comorbidities (cardiovascular, neurological, and metabolic) in order to ultimately develop effective preventive and treatment interventions. Initiatives focusing on partnering with community based organizations, nongovernmental organizations, and local agencies to implement and disseminate effective and cost-effective HIV prevention and treatment intervention services will be fostered.

Training, Infrastructure, and Capacity Building: NIH-sponsored training of domestic and international biomedical, behavioral, and social science HIV researchers represents an overarching priority for NIH HIV/AIDS research. NIH also provides infrastructure and capacity building support as integral aspects of its commitment to carrying out scientifically and ethically sound and highly productive HIV-related research. The evolving AIDS pandemic and the global

expansion of NIH-funded HIV/AIDS research have necessitated the development of research training, and infrastructure and capacity building efforts in many areas, especially in resource-limited settings throughout the world. The NIH-sponsored programs have increased the number of training positions for HIV-related researchers, including domestic and international programs specifically designed to recruit individuals from populations underrepresented in research into research careers and to build research capacity at minority-serving institutions in the United States. Equipment, shared instrumentation, and tissue and specimen repositories are examples of the research infrastructure and capacity building support that NIH provides to strengthen the conduct of AIDS-related research, both domestically and internationally.

Budget Policy:
The FY 2017 President's Budget estimate for Training, Infrastructure, and Capacity Building is $196.855 million, a decrease of $3.118 million or 1.56 percent compared to the FY 2016 Enacted level. NIH will continue to support training programs and infrastructure development for both U.S. and low-and middle income country (LMIC) researchers to build the critical capacity to conduct AIDS research. NIH will continue to provide support for the training of early stage investigators for careers in HIV-related research. NIH also will support efforts to ensure an adequate number of trained intramural AIDS researchers through the AIDS Research Loan Repayment Program and the Intramural AIDS Research Fellowship program.

Information Dissemination: NIH supports innovative initiatives to enhance the dissemination of research findings; develop and distribute state-of-the-art treatment and prevention guidelines; and enhance recruitment and retention of hard-to-reach populations and at-risk individuals in clinical studies. Effective information dissemination approaches are an integral component of successful HIV prevention, treatment, and cure studies, particularly with respect to issues related to adherence to treatment regimens and prevention strategies, and the need to effectively translate in a timely manner biomedical, behavioral, and social science prevention interventions into practice. Continued progress in treatment and prevention research depends on the transfer of current HIV research findings to researchers, providers, policy makers, the public, and HIV-infected and -affected individuals. These groups have varying needs for evidence-based information that is crucial to the achievement of an AIDS-free generation, therefore making it a priority to appropriately tailor the format and content of scientific information for each community. The diversity of the communities makes it imperative that socially- and culturally-sensitive and responsive approaches address the different levels of health literacy and the various methods information is accessed. The flow of information among researchers, providers, and HIV-affected communities represents new opportunities to utilize new and emerging technologies, including mobile applications, to speed the translation of research results into practice and to shape future research directions aligned with the overarching HIV/AIDS research priorities.

Budget Policy:
The FY 2017 President's Budget estimate for Information Dissemination is $38.274 million, a decrease of $0.477 million or 1.23 percent compared to the FY 2016 Enacted level. Resources will continue to support dissemination of clinical trials-related information to ensure recruitment of an adequate number of participants, particularly from populations at risk, including women and racial and ethnic populations in the United States. Funding also will be provided to ensure

that findings from clinical trials and critical federal guidelines on the use of antiretroviral therapy, as well as guidelines for the management of HIV associated complications for adults and children, are continually updated and rapidly disseminated to healthcare providers and patients through the AIDS*info* website (www.aidsinfo.nih.gov). Other initiatives will focus on expanding community organizations, libraries, and the public health workforce to receive pertinent HIV-related information in a timely manner, and developing specialized tools for HIV sequence analysis.

Global Impact of NIH AIDS Research: Research to address the global AIDS pandemic is essential. Since the early days of the pandemic, NIH has supported research in countries significantly affected by HIV/AIDS, beginning in 1983 with a research project in Haiti. The NIH international HIV/AIDS research portfolio has grown to projects in over 100 countries, focused on priority areas relevant for both the host nation and the United States. HIV/AIDS research represents the largest component of the total NIH global research investment. Implementation studies are critical to translating clinical trial results into community-based interventions that can be operational and sustainable in international settings. Most grants and contracts that include international engagement are awarded to U.S.-based investigators who conduct research in collaboration with in-country scientists; some are awarded directly to investigators in international scientific, academic, or medical institutions, as well as international health organizations and agencies. NIH-sponsored HIV/AIDS research also enhances research infrastructure and training programs of scientists and healthcare providers in international settings. NIH has partnered with international funding agencies to jointly fund and manage bilateral initiatives that address HIV prevention and treatment research areas of mutual interest and shared priority. In addition to advancing scientific knowledge and providing new and unique collaborative opportunities for U.S. investigators, these initiatives provide access to populations and cohorts most affected by the AIDS pandemic, as well as complementary scientific expertise, which may not be available in the United States.

AIDS Research Conducted in International Settings

(Dollars in Millions)

FY 2015 Actual	FY 2016 Enacted	FY 2017 PB
$433.834	$431.101	$431.913

Benefits of AIDS Research to Other Areas: NIH's investment in HIV/AIDS research has resulted in critical scientific accomplishments that benefit not only the nearly 37 million HIV-infected individuals around the world, but has also contributed knowledge to the prevention, diagnosis, and treatment of many other diseases and conditions. HIV/AIDS research broadens the overall understanding of immunology, virology, microbiology, molecular biology, and genetics. HIV/AIDS research is helping to unravel the mysteries surrounding other diseases because of the pace of discovery and the unique nature of HIV (i.e. the way the virus enters a cell, causes infection, affects every organ system, and involves a broad range of opportunistic infections, co-morbidities, cancers, and other complications).

HIV/AIDS research continues to make discoveries that can be applied to other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia. HIV immunology and biology research has informed the understanding of inflammation and aging. Research on HIV-associated neurologic and cognitive manifestations

ultimately may benefit millions of patients with Alzheimer's disease and other aging and dementia issues. HIV/AIDS treatment research has led to more effective drugs for multiple bacterial, mycobacterial, and fungal diseases and fostered significant improvements in drug design and delivery technologies that can improve adherence. The treatment of hepatitis C infection, which currently affects more than 185 million people globally, has been revolutionized and curative regimens are now available. AIDS research has led to the development of new models to test treatments for other diseases in faster, more efficient, and more inclusive clinical trials. Experience gained from the development of protease inhibitors to treat HIV infection, are being applied to treat develop antiviral therapies to treat cytomegalovirus, which is a significant cause of birth defects. Recent observational studies suggest that HIV infection and its treatment lessens the population risk of getting multiple sclerosis (MS). The relationship between this observation and the cause may open new avenues for the care and treatment of MS. AIDS research also has advanced understanding of the relationship between viruses and cancer. New investments in HIV/AIDS research will continue to fuel biomedical advances and breakthroughs that will have profound benefits far beyond the AIDS pandemic.

Conclusion: While significant groundbreaking scientific advances have resulted from NIH's investment in HIV/AIDS research, we are facing unprecedented scientific opportunities. NIH's continued leadership and commitment to build on these advances is essential to successfully develop a safe and effective AIDS vaccine, develop strategies to cure AIDS, and ultimately, achieve an AIDS free generation and an end to the AIDS pandemic. This budget request provides the essential resources to achieving these goals.