

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Trans-NIH AIDS Research Budget

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Prevention Science Working Group
Therapeutics Research Working Group
Microbicides Research Working Group
Genomics/Genetics Research Working Group
AIDS and Aging Working Group
Cure Research Working Group

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

Institute / Center	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
NCI	\$261,550	\$269,923	\$272,212	\$2,289
NHLBI	64,046	64,218	64,559	341
NIDCR	18,896	18,465	17,873	-592
NIDDK	29,153	30,031	30,354	323
NINDS	44,136	45,465	44,223	-1,242
NIAID	1,481,620	1,567,913	1,590,026	22,113
NIGMS	61,415	64,263	64,956	693
NICHD	136,507	140,616	142,055	1,439
NEI	2,748	1,747	1,360	-387
NIEHS	5,028	5,179	5,151	-28
NIA	5,305	5,465	5,468	3
NIAMS	4,639	4,779	4,753	-26
NIDCD	1,768	1,821	1,811	-10
NIMH	179,449	157,493	157,005	-488
NIDA	300,749	301,532	300,714	-818
NIAAA	26,732	27,537	27,413	-124
NINR	11,908	12,266	12,202	-64
NHGRI	6,716	6,918	6,380	-538
NIBIB	3,484	1,229	713	-516
NIMHD	19,259	19,839	19,607	-232
NCCAM	1,516	1,562	1,415	-147
NCATS	64,360	66,297	64,287	-2,010
FIC	22,833	23,520	23,463	-57
NLM	7,220	7,937	7,897	-40
OD				
OAR	60,718	61,923	61,923	--
ORIP	76,110	77,153	77,153	--
Subtotal, OD	136,828	139,076	139,076	--
TOTAL, NIH	\$2,897,865	\$2,985,091	\$3,004,973	\$19,882

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS

(Dollars in Thousands)

MECHANISM	FY 2013 Actual		FY 2014 Enacted ²		FY 2015 President's Budget		FY 2015 +/- FY 2014	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
<u>Research Projects:</u>								
Noncompeting	1,690	\$1,096,653	1,528	\$962,093	1,529	\$1,193,973	1	\$231,880
Administrative Supplements	(99)	100,494	(47)	16,610	(43)	16,010	(-4)	-600
Competing	571	256,261	712	609,380	741	402,205	29	-207,175
Subtotal, RPGs	2,261	\$1,453,408	2,240	\$1,588,083	2,270	\$1,612,188	30	\$24,105
SBIR/STTR	68	34,484	62	32,945	61	33,770	-1	825
Research Project Grants	2,329	\$1,487,892	2,302	\$1,621,028	2,331	\$1,645,958	29	\$24,930
<u>Research Centers:</u>								
Specialized/Comprehensive	62	\$130,504	59	\$127,380	59	\$123,493	--	-\$3,887
Clinical Research	2	55,673	2	57,209	2	55,617	--	-1,592
Biotechnology	0	759	0	778	0	720	--	-58
Comparative Medicine	16	56,560	16	56,703	16	56,341	--	-362
Research Centers in Minority Institutions	14	13,064	14	13,077	14	13,077	--	--
Research Centers	94	\$256,560	91	\$255,147	91	\$249,248	--	-\$5,899
<u>Other Research:</u>								
Research Careers	237	\$42,034	235	\$42,326	229	\$42,068	-6	-\$258
Cancer Education	0	0	0	0	0	0	--	--
Cooperative Clinical Research	8	17,550	8	17,550	8	17,550	--	--
Biomedical Research Support	1	2,672	1	2,672	1	2,672	--	--
Minority Biomedical Research Support	1	348	1	359	1	359	--	--
Other	152	61,981	155	60,147	152	59,440	-3	-707
Other Research	399	\$124,585	400	\$123,054	391	\$122,089	-9	-\$965
Total Research Grants	2,822	\$1,869,037	2,793	\$1,999,229	2,813	\$2,017,295	20	\$18,066
<u>Ruth L. Kirschstein Training Awards:</u>	<u>FTIPs</u>		<u>FTIPs</u>		<u>FTIPs</u>			
Individual Awards	95	\$3,993	93	\$4,090	91	\$3,993	-2	-\$97
Institutional Awards	642	33,190	644	33,690	644	33,710	--	20
Total Research Training	737	\$37,183	737	\$37,780	735	\$37,703	-2	-\$77
Research & Develop. Contracts (SBIR/STTR) (non-add) ¹	107 (3)	\$488,608 (688)	102 (6)	\$434,001 (1,659)	102 (7)	\$433,876 (4,047)	-- (1)	-\$125 (2,388)
Intramural Research		\$325,775		\$332,196		\$333,463		\$1,267
Res. Management and Support		116,544		119,962		120,713		751
Res. Management & Support (SBIR Admin) (non-add)								
Office of the Director - Appropriation ¹		(136,828)		(139,076)		(139,076)		--
Office of the Director - Other		60,718		61,923		61,923		--
ORIP (non-add) ^{1,3}		(76,110)		(77,153)		(77,153)		--
Total, NIH Discretionary B.A.		\$2,897,865		\$2,985,091		\$3,004,973		\$19,882

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

² The amounts in the FY 2014 column take into account funding reallocations, and therefore may not add to the total budget authority reflected herein.

³ Number of grants and dollar amounts for the ORIP component of the OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriation also is noted as a non-add since these funds are accounted for under OD-Other.

NATIONAL INSTITUTES OF HEALTH Office of AIDS Research Budget Authority by Activity (Dollars in Thousands)						
Area of Emphasis	FY 2011 Actual	FY 2012 Actual	FY 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015 +/- FY 2014
HIV Microbicides	\$120,982	\$129,919	\$111,240	\$113,118	\$112,647	-\$471
Vaccines	548,834	556,613	518,170	530,866	535,187	4,321
Behavioral and Social Science	412,163	420,084	397,377	413,295	418,503	5,208
Etiology and Pathogenesis	730,978	668,244	625,027	664,954	693,985	29,031
Therapeutics						
<i>Therapeutics as Prevention</i>	65,064	56,561	69,375	64,618	66,391	1,773
<i>Drug Discovery, Development, and Treatment</i>	<u>615,475</u>	<u>650,059</u>	<u>632,123</u>	<u>663,839</u>	<u>652,157</u>	<u>-11,682</u>
Total, Therapeutics	680,539	706,620	701,498	728,457	718,548	-9,909
Natural History and Epidemiology	278,998	257,973	243,454	225,528	219,490	-6,038
Training, Infrastructure, and Capacity Building	232,624	280,775	261,921	269,912	267,139	-2,773
Information Dissemination	54,159	54,567	39,178	38,961	39,474	513
Total	\$3,059,277	\$3,074,795	\$2,897,865	\$2,985,091	\$3,004,973	\$19,882

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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 2013 Actual	FY 2014 Enacted	FY 2015 President's Budget	FY 2015+/- FY 2014
\$2,897,865,297	\$2,985,091,000	\$3,004,973,000	\$19,882,000

DIRECTOR'S OVERVIEW

Groundbreaking Accomplishments: In the three decades since AIDS was first reported, the NIH has been the global leader in research to understand, prevent, diagnose, and treat HIV and its many related conditions. Recent scientific advances resulting from NIH-funded research represent a critical moment for AIDS research. New avenues for discovery have been identified, providing possibilities for the development of new strategies to prevent, treat, and potentially cure HIV. Recent accomplishments include:

- Development of new treatments for many HIV-associated co-infections, co-morbidities, malignancies, and clinical manifestations;
- Development of new strategies for the prevention of mother-to-child transmission (MTCT), which have resulted in dramatic decreases in perinatal HIV in the U.S., where now fewer than 100 babies a year are born with HIV infection;
- Demonstration of the first proof of concept that a vaccine can prevent HIV infection and identification of potential immune markers for protection;
- Discovery of more than 20 potent human antibodies that can stop up to 95 percent of known global HIV strains from infecting human cells in the laboratory;
- Demonstration that the use of antiretroviral therapy by infected individuals can dramatically reduce HIV transmission to an uninfected partner;
- Demonstration of the effectiveness of pre-exposure prophylaxis (PrEP), the use of antiretroviral treatment regimens by uninfected individuals to reduce their risk of HIV acquisition;
- Discovery that genetic variants may play a role in enabling some individuals, known as “elite controllers,” to control HIV infection without therapy;
- Critical basic science discoveries that continue to provide the foundation for novel research;
- Advances in basic and treatment research aimed at eliminating viral reservoirs in the body that for the first time are leading scientists to design and conduct research aimed at a cure for HIV/AIDS.

In just the past few months, NIH intramural and extramural researchers have produced two new exciting advances. NIH researchers published the results of studies utilizing potent human

neutralizing antibodies that successfully suppressed a form of HIV in primates. This important research could potentially result in a new form of treatment for HIV that could be used as an adjunct to antiretroviral therapy and could lead to opportunities for novel research to treat and potentially cure HIV. NIH-sponsored researchers also have made tremendous strides in producing and analyzing proteins that may provide an important new pathway in AIDS vaccine design.

NIH is leading global research efforts to capitalize on all of these advances, move science forward, and begin to turn the tide against this pandemic. Despite this progress, the HIV/AIDS pandemic will remain the most serious global public health crisis of our time until better, more effective, and affordable prevention and treatment regimens—and eventually a cure—are developed and available around the world.

Mission: The 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 AIDS-related research supported by every NIH Institute and Center (IC). OAR coordinates the scientific, budgetary, and policy elements of the trans-NIH research program on AIDS and its wide spectrum of associated malignancies, co-infections, and clinical complications. Through its unique trans-NIH planning, budget, and evaluation processes, OAR identifies the highest priority areas of scientific opportunity, enhances collaboration, and minimizes duplication to invest precious research dollars effectively. The OAR has shifted resources across ICs and areas of science as needed to address these priorities and the changing clinical profile of the pandemic.

Challenges and Opportunities for FY 2015: The key scientific priorities for NIH AIDS research address the goals of the President’s National HIV/AIDS Strategy as well as the President’s Executive Order about the HIV Care Continuum. The priorities are also aligned with the NIH Director’s themes as outlined below. OAR will target funding on:

- **Today’s Basic Science for Tomorrow’s Breakthroughs:** A key priority is basic research on HIV that will underpin further development of critically needed *vaccines, microbicides, and other prevention strategies*. Another important area will focus on research related to the potential for a *cure or lifelong remission* of HIV infection, including studies on viral persistence, latency, reactivation, and eradication.
- **Precision Medicine:** NIH will continue to invest in research to *develop better, less toxic, longer acting, and sustained anti-HIV treatments* and to investigate how genetic determinants, sex, gender, race, age, nutritional status, treatment during pregnancy, and other factors interact to affect treatment success or failure. Research on behavioral issues, such as the role of stigma and adherence to treatment or prevention strategies, also is important, particularly to address the HIV Care Continuum. Another key priority in this area is research on *co-morbidities and disease progression*, including treatment and prevention of HIV-related co-infections, malignancies, and neurological, cardiovascular, and metabolic complications.

- **Nurturing Talent and Innovation:** NIH will utilize resources to train the next generation of AIDS researchers around the world to foster collaboration and innovation in AIDS research, with a particular emphasis on *research toward a cure*.

Overall Budget Policy:

To address these critical AIDS research priorities, the FY 2015 President's Budget estimate for the trans-NIH AIDS research program is \$3,004.973 million, an increase of \$19.882 million or 0.7 percent above the FY 2014 Enacted level. This amount includes the total trans-NIH support for intramural and extramural research for basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the wide spectrum of AIDS-associated malignancies, opportunistic infections, co-infections, and clinical complications; as well as research management support; research centers; and training and infrastructure. This request reflects the shifting of funds across ICs to address new and exciting scientific opportunities in AIDS research. These shifts reflect the scientific priorities identified through the unique annual trans-NIH strategic planning portfolio analysis, and budget processes and address the evolving clinical profile of the epidemic, changing demographics, and most recent scientific advances. In this budget request, OAR has provided increased funding to support: high priority basic research (etiology and pathogenesis) that provides the underlying foundation for all HIV research, including prevention and treatment of HIV and research to better understand disease progression and HIV-related co-morbidities. This fundamental research also includes the first year of a three-year commitment to increase NIH research toward a cure. Another major priority is prevention research, particularly new opportunities in the development of vaccines. An increase is provided for behavioral and social sciences research, particularly research to better understand issues of adherence to both prevention and treatment strategies. In order to provide those increases to support the highest priorities and new scientific opportunities, OAR has had to reduce and redirect funds from other scientific areas within AIDS research.

PROGRAM DESCRIPTIONS AND ACCOMPLISHMENTS

Trans-NIH Strategic Plan and Budget: This budget request is informed by the FY 2015 Trans-NIH Plan for HIV-Related Research (Strategic Plan). The OAR trans-NIH planning process involves government and non-government experts and representatives from community constituency groups. This process results in the identification of overarching AIDS-research priorities and specific research objectives and strategies. The OAR Advisory Council has also reaffirmed the key scientific priorities. OAR is mandated to develop the annual trans-NIH AIDS research budget in partnership with the ICs and explicitly tied to the objectives of the Strategic Plan. OAR's AIDS research allocation to each IC is not based on a formula, but on the scientific priorities and objectives of the annual Strategic Plan, taking into account the current scientific opportunities and priorities, the evolving clinical profile of the epidemic, and the IC's capacity to absorb and expend resources for the most meritorious science. This process reduces redundancy, promotes harmonization, and assures cross-Institute collaboration to conduct and support research in domestic and international settings. Specific programmatic areas include:

HIV MICROBICIDES

A safe and effective microbicide will be an important asset to the HIV prevention tool kit. Microbicides are products, including antiretroviral drugs and other agents, which could be applied topically or injected to prevent acquisition of HIV and other sexually transmitted infections. Microbicides could be used alone or in combination with other strategies. NIH supports a comprehensive and innovative microbicide research program that includes the screening, discovery, development, preclinical testing, and clinical evaluation of microbicide candidates. NIH supports basic science research aimed at understanding how HIV crosses mucosal membranes and infects cells. In addition, NIH supports behavioral and social science research on adherence to, and the acceptability and use of microbicides among different 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 product into community prevention practices. Basic science and clinical studies have shown promise for the use of antiretroviral (ARV)-based microbicides as HIV prevention strategies. Follow-up studies are underway or being developed to test different ARV- and non-ARV-based products, microbicides combined with a contraceptive for multipurpose prevention, and microbicides combined with antimicrobial agents to prevent HIV and other sexually transmitted infections (STIs). Microbicide formulations and new technologies that enhance adherence, such as injectable products, nanofibers, films, suppositories, and intravaginal rings also are being developed and studied.

Budget Policy:

The FY 2015 President's Budget request for Microbicides research is \$112.647 million, a decrease of \$0.471 million or 0.4 percent below the FY 2014 Enacted level for this area of prevention research. In FY 2015, NIH will continue to support the discovery, design, development, formulation, and evaluation of microbicide candidates. Key ongoing activities include support for the NIH-funded Microbicide Trials Network (MTN) and the necessary infrastructure to conduct basic research and microbicide clinical trials. Research activities will utilize this infrastructure to build on recent scientific advances and develop innovative, novel, and high risk-high reward approaches for the discovery, development, formulation, and testing of microbicide candidates and delivery systems. Research activities also will focus on the development and testing of multi-purpose prevention technologies (MPTs) that prevent HIV and other STIs or HIV and pregnancy; and on the continued study of animal and tissue models designed to enhance understanding of the mechanisms of HIV infection and assist safety and efficacy evaluations of candidate microbicide products. 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 and research on ethics, adherence, and other behavioral and social science issues that can impact clinical trials and microbicide use. Through a number of trans-governmental working groups and non-governmental expert consultations, OAR will continue to foster coordination and

collaboration in innovative microbicide research leading to the development and testing of novel potential candidates that can prevent HIV transmission and acquisition.

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. Information gained from these studies is being used to inform the design and development of novel vaccine strategies. 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. Samples from the HVTN 505 trial in the U.S. with DNA and adenovirus vectors are being subjected to similar analyses to understand why that vaccine strategy failed to protect against HIV acquisition. To build on the knowledge gained from these studies, clinical trials in other populations and in other parts of the world with new and potentially improved products and alternative vectors have been designed and are currently underway. Recent data from several phase I and II vaccine clinical studies present new scientific opportunities for the development of improved HIV vaccine candidates.

Budget Policy:

The FY 2015 President's Budget request for Vaccine research is \$535.187 million, an increase of \$4.321 million or 0.8 percent above the FY 2014 Enacted level. Innovative basic HIV vaccine research studies will be supported to inform the development of new vaccine concepts that might prevent HIV infection more efficiently than vaccines already tested. In FY 2015, NIH will fund additional development of improved animal models including new models for vaccine challenge studies in non-human primates to test vaccine concepts and to aid informed testing of HIV vaccine candidates in clinical trials. NIH will provide support for new initiatives to integrate systems biology with HIV vaccine discovery; and will fund additional research to develop new tests to measure immune responses to the HIV vaccine candidate that will more closely predict outcomes of parallel preclinical animal and human clinical studies. Resources will be directed toward the development and testing of improved vaccine candidates in additional clinical studies, both in the U.S. and abroad, building on the early protection observed in the previous Phase III vaccine trial in Thailand and a deeper understanding of the failure of the recent HVTN 505 trial to demonstrate protection in clinical trial participants in the U.S. To ensure that these new opportunities can be pursued, a realignment of resources will be needed. This budget request reflects OAR's redirection of funds from other scientific areas to support critical vaccine research opportunities.

BEHAVIORAL AND SOCIAL SCIENCE

As studies continue to define a role for the use of antiretroviral medications for HIV prevention, NIH is supporting research to understand how these drugs can best be used for prevention in specific populations and social contexts. NIH will continue to study ways to change those 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. Investigations are not only focused on individual-level variables, but on social and structural issues, such as the role of stigma, housing, employment, health care access, and interpersonal networks. Studies have suggested that modifying these variables can promote early access to medical care, reduce costs, extend life expectancy, and improve quality of life. NIH will continue to develop new research methods that can be applied to behavioral and social science studies, as well as the integration of biomedical and behavioral strategies in clinical investigations. These include approaches to increase recruitment into clinical trials; enhance statistical analyses of behaviors, such as alcohol use, that can affect medication studies; and identify behavioral issues relevant to genetic or genomic studies.

Budget Policy:

The FY 2015 President's Budget request for Behavioral and Social Science is \$418.503 million, an increase of \$5.208 million or 1.3 percent above the FY 2014 Enacted level. NIH will shift its investments within the area of behavioral and social sciences to keep pace with the increasing integration of biomedical and behavioral perspectives, the success of antiretroviral medications in both prevention and treatment, and the key role of adherence to this success. To achieve a more integrated portfolio, attention will be given to improving the implementation of therapies in specific populations and social contexts. Social variables, such as stigma, and structural variables to improve access to prevention and treatment resources will also be addressed, and a strong emphasis on basic science to understand risk behaviors from both a social and biomedical (e.g., neurophysiologic and genomic) perspective. NIH will support initiatives to better understand the multiple factors related to adherence, utilizing novel ways to ensure that patients take their medications and use prevention strategies appropriately.

ETIOLOGY AND PATHOGENESIS

NIH supports a comprehensive portfolio of research focused on the transmission, acquisition, establishment, and maintenance of HIV infection and the causes of its associated profound immune deficiency and severe clinical complications. Research on basic HIV biology and AIDS pathogenesis has revolutionized the design of drugs, methodologies for diagnosis of HIV infection, and tools for monitoring disease progression and the safety and effectiveness of antiviral 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, and other clinical complications, malignancies, and co-infections (including tuberculosis [TB] and hepatitis C). Research examining the genetic determinants associated with HIV susceptibility, disease progression, and treatment response is also needed. These studies may lead to the development of customized therapeutic and preventive regimens formulated for an individual patient based on his or her genetic sequence. 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 could 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.

Budget Policy:

The FY 2015 President's Budget request for the basic research area of Etiology and Pathogenesis is \$693.985 million, an increase of \$29.031 million or 4.4 percent above the FY 2014 Enacted level. Studies related to the development of microbicides and vaccines, as well as research toward a cure have revealed gaps in knowledge and understanding of HIV etiology and pathogenesis, particularly with regard to host immune responses, how HIV interacts with and crosses host target surfaces, and the establishment and maintenance of latent viral reservoirs in the body (HIV persistence). NIH will provide increased resources for research on the biology of HIV transmission and pathogenesis studies including research on HIV-associated immune system dysfunction and chronic inflammation. NIH will support studies of clinical complications, such as HIV-associated co-infections, malignancies, premature aging, cardiovascular disease, neurological and metabolic disorders. Funds will be provided for research to better understand the differences in HIV transmission, treatment, and progression in women compared to men as well as the unique clinical manifestations of HIV disease in women. An important area will focus on research related to the potential for a cure or lifelong remission of HIV infection, including studies on viral persistence, latency, and reactivation. On World

AIDS Day 2013, the President announced that NIH will redirect \$100 million over the next three fiscal years (FY 2015-2017) to research towards a cure. OAR will launch that new initiative with an investment of \$15 million in cure research in FY 2015. OAR jump-started the initiative with an investment of an additional \$10 million in FY 2014.

Program Portrait: Research Toward a Cure: Eradication of Viral Reservoirs

FY 2014 Level: \$ 88.5 million

FY 2015 Level: \$104.9 million

Change: \$+16.4 million

Research related to the potential for a cure or lifelong remission of HIV infection is a key NIH research priority, which currently involves research across a number of areas. NIH plans to increase this area of research over the next three fiscal years focused on:

- **Pathogenesis studies:** Basic research on viral reservoirs, viral latency, and viral persistence, including studies on genetic factors associated with reactivation of the virus, and other barriers to HIV eradication.
- **Animal models:** Identification and testing of various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.
- **Drug development and preclinical testing:** Programs to develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system and brain.
- **Clinical trials:** Studies to evaluate lead compounds, drug regimens, and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.
- **Therapeutic vaccines:** Design and testing of vaccines that would be capable of suppressing viral replication and preventing disease progression.
- **Adherence/compliance:** Development and testing of strategies to maintain adherence/compliance to treatment, in order to improve treatment outcomes and reduce the risk of developing HIV drug resistance.

THERAPEUTICS

Drug Discovery, Development and Treatment: Antiretroviral treatment (ART) has resulted in improved immune function in patients who are able to adhere to the treatment regimens and tolerate the toxicities and side effects associated with antiretroviral drugs. ART also has delayed the progression of HIV disease to the development of AIDS. Unfortunately, the treatment is beginning to fail in an increasing number of patients who have been on antiretroviral therapy. These patients are experiencing serious drug toxicities and

Improved Therapies for Long-Term Survival

NIH researchers are working to:

- Develop innovative therapies and novel cell-, gene-, and immune-based approaches to control and eradicate HIV infection;
- Develop new formulations, including long-acting therapies;
- Identify new drug targets based on the structure of HIV/host complexes;
- Delineate the interaction of aging and AIDS, including neurological, cardiovascular, and metabolic complications, as well as issues of frailty;
- Discover and develop improved therapies for AIDS-defining and non-AIDS-defining malignancies; and
- Discover the next generation of drugs that may be used in potential “therapeutics as prevention” strategies.

developing drug resistance. Recent epidemiologic studies have shown that the incidence of co-infections, co-morbidities, AIDS-defining and non-AIDS defining malignancies, and complications associated with long-term HIV disease and ART are increasing. These include tuberculosis, Hepatitis C, metabolic disorders, cardiovascular disease, conditions associated with aging, and neurologic and neurocognitive disorders. 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 undetectable viral load, to overcome drug resistance and treatment failure, and to prevent and treat HIV-associated co-infections, co-morbidities, and other complications. The program supports cure research with a focus on developing drugs and cell- and gene-based strategies that can target and eradicate persistent viral reservoirs in various cells, tissues, and organ systems, including the central nervous system and brain. This program also is supporting pre-clinical trials of innovative strategies to eliminate viral reservoirs including testing therapeutic anti-HIV monoclonal antibodies with and without antiretroviral drugs.

Therapeutics as Prevention: A critical new 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 that treatment of HIV-infected pregnant women could significantly reduce transmission of HIV from mother to child. Recent groundbreaking studies have demonstrated the successful use of antiretrovirals to prevent transmission of HIV in specific populations. Clinical results from a large NIH-sponsored international clinical trial (HIV Prevention Trials Network [HPTN] 052) showed that early initiation of antiretroviral treatment of HIV-infected heterosexual individuals resulted in a 96 percent reduction in sexual transmission of HIV to their uninfected partner. Another major NIH-sponsored clinical trial, the Chemoprophylaxis for HIV Prevention in Men study, also known as iPrEx, demonstrated that daily use of an antiretroviral drug by some high-risk uninfected men could reduce their risk of acquiring HIV. The findings from this study showed proof of concept and the effectiveness of a novel HIV prevention strategy known as Pre-Exposure Prophylaxis (PrEP). Recent studies have shown PrEP to be effective in preventing HIV acquisition among two at-risk populations: women in heterosexual discordant couples and injection drug users. NIH supports ongoing basic, translational, clinical, and implementation research to develop combinations of antiretroviral drugs and compounds that can be used in sustained release formulations that can be used in potential new PrEP strategies; test PrEP in high risk uninfected populations, including adolescents; evaluate post-exposure prophylaxis, the use of ART 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 2015 President’s Budget request for Therapeutics research is \$718.548 million, a decrease of \$9.909 million or 1.4 percent below the FY 2014 Enacted level. The overall funding for therapeutics research will be reduced to allow for increased funding for other areas. A portion of the funds from expiring grants and contracts for therapeutics research will be reallocated to studies on treatment and prevention of HIV-associated co-infections and co-morbidities and to support crucial basic research on targeting and eradicating HIV reservoirs.

Resources within the area of Therapeutics also will be directed to support: recompetition of the AIDS Malignancy Consortium and Pediatric HIV/AIDS Cohort Study; development of new combinations of anti-HIV drugs and sustained release formulations and delivery systems to maintain viral suppression; several initiatives to develop and test new therapeutic monoclonal antibodies with and without antiviral drugs; expansion of programs targeting innovative approaches to develop and evaluate novel cell-, gene-, and immune-based approaches to control and eradicate HIV infection that may lead to a cure; identifying new drug targets based on the structure of HIV/host complexes; delineating the interaction of aging and neuro-AIDS; developing new strategies to test and treat patients with HIV-related co-infections, including Hepatitis C virus and tuberculosis; and conducting clinical studies on cardiovascular complications of HIV disease and ART. Increased funding will be provided for the area of *Therapeutics as Prevention*, including discovery and testing the next generation of sustained release formulations of antiretroviral drugs that may be used in potential new strategies for PrEP; treatment of HIV-infected individuals to prevent transmission; post-exposure prevention; and new antiretroviral drug regimens to prevent mother-to-child transmission, including transmission through breastfeeding.

NATURAL HISTORY AND EPIDEMIOLOGY

Natural history and epidemiologic research on HIV/AIDS is critical to the monitoring of 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. Multi-site epidemiologic studies in the U.S. are identifying new HIV-related co-morbidities and helping to differentiate effects related to antiretroviral treatment from those related to HIV disease. As the AIDS epidemic continues to evolve, there is a crucial need for epidemiologic studies in domestic and international settings. NIH supports a comprehensive research portfolio in both settings 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, 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 U.S.; 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 U.S. as well as individuals over the age of 50. Research on HIV-related health disparities and their impact on treatment access and effectiveness, as well as HIV prevention, will continue to be an NIH AIDS research priority.

Budget Policy:

The FY 2015 President's Budget request for Natural History and Epidemiology is \$219.490 million, a decrease of \$6.038 million or 2.7 percent below the FY 2014 Enacted level. The funding reduction in this area will allow OAR to shift these funds to key priorities within prevention research and research toward a cure. However, NIH will continue to use existing

networks and research cohorts to support high-priority epidemiology studies of populations most at risk, including men who have sex with men (MSM), especially MSM of color; women; adolescents; and individuals over fifty years of age who are aging with HIV. Population studies on the long-term effects of HIV disease and its treatment will be emphasized as well as studies of non-communicable disease co-morbidities that have become more commonly diagnosed in HIV-infected people under HIV treatment. Epidemiologic research also will include the development of novel trans-disciplinary methods to examine the prevention, testing, and treatment cascade by integration of data from electronic medical records, observational studies, clinical trials and simulation, mathematical modeling, and molecular epidemiology. Resources will be provided for studies of HIV implementation science, including those that advance new methodologies and studies that maximize program effectiveness by addressing organizational and system-level barriers to the scale-up of prevention and treatment interventions. Studies also will be supported that formally evaluate the economic impact and cost-effectiveness of diverse interventions strategies in different regions and circumstances.

TRAINING, INFRASTRUCTURE, AND CAPACITY BUILDING

NIH supports the training of domestic and international biomedical and behavioral HIV researchers. 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 expansion of NIH-funded HIV research globally has necessitated the development of research training and infrastructure and capacity building efforts in many resource-limited settings throughout the world. NIH-funded 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 U.S. 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 2015 President's Budget estimate for Training, Infrastructure, and Capacity Building is \$267.139 million, a decrease of \$2.773 million or 1.0 percent below the FY 2014 Enacted level. NIH will continue to support training programs and infrastructure development for both U.S. and international researchers to build the critical capacity to conduct AIDS research in the United States and in developing countries. NIH will continue to build capacity for the development of animal models for AIDS research by continuing to support ongoing efforts to increase the supply of non-human primates and develop other animal models. NIH 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 initiatives to enhance dissemination of research findings; develop and distribute state-of-the-art treatment and prevention guidelines; and enhance recruitment and retention of participants in clinical studies. Effective information dissemination approaches are an integral component of HIV prevention and treatment efforts. These efforts are crucial in light of the advent of new and complex antiretroviral treatment regimens, issues related to adherence to prescribed treatments, and the need to translate behavioral and social prevention approaches into practice. The changing pandemic and the increasing number of new infections in specific population groups in the U.S. underscore the need to disseminate HIV research findings and other related information to communities at risk, such as racial and ethnic populations, women, older individuals, and men who have sex with men. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to use new and emerging technologies to speed the translation of research results into practice and to shape future research directions.

Budget Policy:

The FY 2015 President's Budget estimate for Information Dissemination is \$39.474 million, an increase of \$0.513 million or 1.3 percent above the FY 2014 Enacted level. As the number and complexity of clinical studies increases, resources must be invested in clinical trials-related information dissemination 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 clinical trial information and critical federal guidelines on the use of antiretroviral therapy, as well as guidelines for the management of HIV complications for adults and children, are updated regularly and disseminated widely to healthcare providers and patients through the *AIDSinfo* website (www.aidsinfo.nih.gov).

Global Impact of NIH AIDS Research: Research to address the global pandemic is essential. AIDS research represents the largest component of the total NIH global research investment. Since the early days of the epidemic, NIH has maintained a strong international AIDS research portfolio that has grown to include projects in approximately 100 countries around the world. NIH AIDS research studies are designed so that the results are relevant for both the host nation and the U.S. These research programs also enhance research infrastructure and training of in-country scientists and healthcare providers. New collaborations have been designed to improve both medical and nursing education as a mechanism to build a cadre of global health leaders. Most of these grants and contracts are awarded to U.S.-based investigators to conduct research in collaboration with in-country scientists; some are awarded directly to investigators in international scientific, academic, or medical institutions.

AIDS Research Conducted in International Settings
(Dollars in Millions)

FY 2013 Actual	FY 2014 Enacted	FY 2015 PB
\$389.166	\$ 375.826	\$375.870

Benefits of AIDS Research to Other Areas: It is essential to point out that AIDS research also pays extensive dividends in many other areas of biomedical research, including in the prevention, diagnosis, and treatment of many other diseases. It deepens our understanding of immunology, virology, microbiology, molecular biology, and genetics. AIDS research is helping to unravel the mysteries surrounding so many 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 unleashes a myriad of opportunistic infections, co-morbidities, cancers, and other complications. 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. AIDS treatment research has led to more effective drugs for multiple bacterial, mycobacterial, and fungal diseases and fostered significant improvements in drug design technologies. 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. Drugs developed to prevent and treat AIDS-associated opportunistic infections also now benefit patients undergoing cancer chemotherapy and patients receiving anti-transplant rejection therapy. AIDS research also has advanced understanding of the relationship between viruses and cancer. New investments in AIDS research will continue to fuel biomedical advances and breakthroughs that will have profound benefits far beyond the AIDS pandemic.

Conclusion: Despite the groundbreaking scientific advances that have resulted from the NIH investment in AIDS research, many serious challenges lie ahead. There is little doubt that the AIDS pandemic will continue to impact virtually every nation in the world for decades to come. In light of this reality, the U.S. national commitment to AIDS research remains strong. The NIH will continue to build on this important moment in science and to support critical research to find new tools to turn the tide in the fight against this pandemic so that we can all once again live in a world without AIDS.