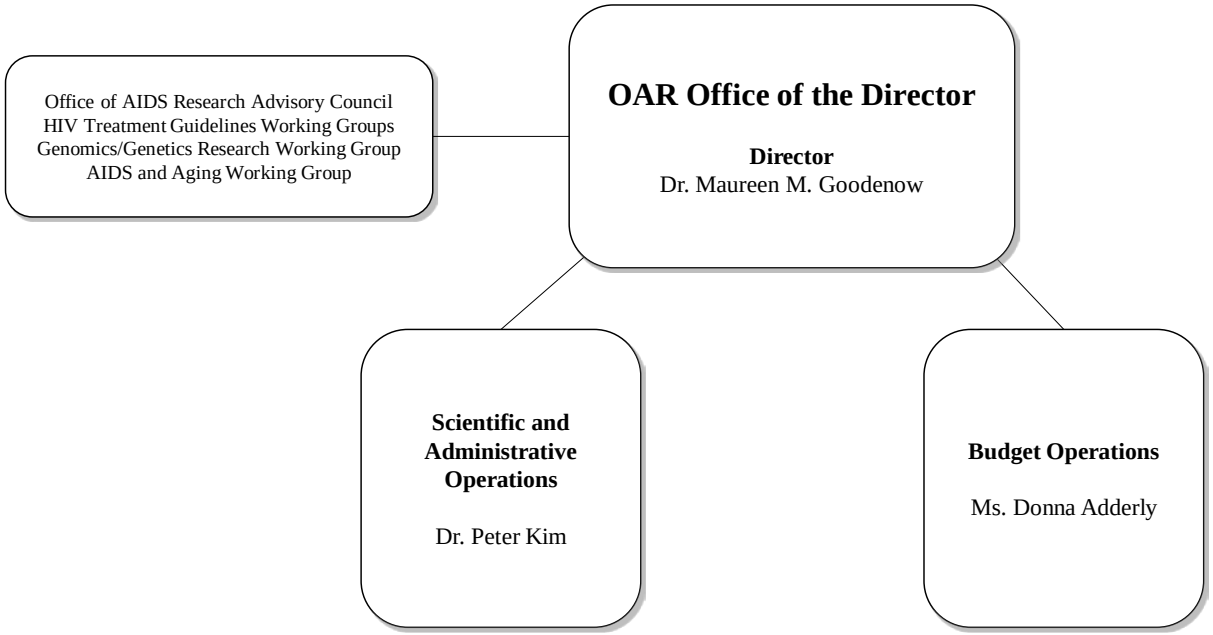
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Trans-NIH HIV/AIDS Research Budget


Office of AIDS Research Advisory Council
HIV Treatment Guidelines Working Groups
Genomics/Genetics Research Working Group
AIDS and Aging Working Group
OAR Office of the Director
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NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Institute and Center
(Dollars in Thousands)

Institute / Center	FY 2016 Actual	FY 2017 Annualized Continuing Resolution	FY 2018 President's Budget	FY 2018 +/- FY 2017
NCI	$266,422	$267,105	$195,382	-$71,723
NHLBI	67,020	68,894	54,724	-14,170
NIDCR	18,015	20,163	14,167	-5,996
NIDDK	29,471	31,458	21,832	-9,626
NINDS	46,536	47,405	35,021	-12,384
NIAID	1,663,823	1,575,054	1,420,164	-154,890
NIGMS	53,194	52,730	41,273	-11,457
NICHD	144,736	145,912	113,339	-32,573
NEI	925	8,813	-	-8,813
NIEHS	5,342	5,501	4,201	-1,300
NIA	5,637	7,568	6,003	-1,565
NIAMS	4,587	5,056	3,607	-1,449
NIDCD	1,878	1,969	1,477	-492
NIMH	161,289	190,643	127,284	-63,359
NIDA	294,244	320,571	217,324	-103,247
NIAAA	28,404	28,604	22,336	-6,268
NINR	12,180	12,729	9,578	-3,151
NHGRI	1,531	7,246	722	-6,524
NIBIB	395	3,677	182	-3,495
NIMHD	21,674	20,673	15,865	-4,808
NCCIH	777	1,622	611	-1,011
NCATS	-	-	-	-
FIC	24,083	24,367	-	-24,367
NLM	8,822	7,787	6,938	-849
OD				
OAR	62,256	61,805	58,348	-3,457
ORIP	76,820	77,006	69,802	-7,204
Subtotal, OD	139,076	138,811	128,150	-10,661
TOTAL, NIH	**$3,000,061**	**$2,994,358**	**$2,440,180**	**-$554,178**

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

Overarching Priorities	FY 2014 Actual	FY 2015 Actual	FY 2016 Actual	FY 2017 Annualized Continuing Resolution	FY 2018 Presidents Budget	FY 2018 +/- FY 2017
Vaccine Research and Reducing the Incidence of HIV/AIDS	$1,057,257	$1,015,701	$1,042,552	$1,026,913	$860,412	-$166,501
Next Generation Therapies	535,391	587,432	478,335	487,255	380,097	-107,158
Research and Devlop a Cure for HIV/AIDS [1/]	---	161,045	230,653	212,250	192,608	-19,642
Improve Treatments for HIV-associated Comorbidities and Co-infections	600,646	585,909	564,094	570,327	467,596	-102,731
Crosscutting--Basic Research, Health Disparities, and Research Training	784,285	649,974	684,427	697,613	539,467	-158,146
Total	$2,977,579	$3,000,061	$3,000,061	$2,994,358	$2,440,180	-$554,178

[1/] Beginning in FY 2017, Research and Develop a Cure for HIV/AIDS became a separate activity. Dollars for Develop a Cure for HIV/AIDS were previously included within other science areas, such as Next Generation Therapies, Crosscutting--Basic Research, and Vaccine Research and Reducing Incidence of HIV/AIDS. The FY 2015 and FY 2016 amounts are comparable budget figures.

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 2016 Actual	FY 2017 Annualized Continuing Resolution	FY 2018 President's Budget	FY 2018+/- FY 2017
$3,000,061,000	$2,994,358,000	$2,440,180,000	-$554,178,000

Director's Overview

Since the first discovery of the human immunodeficiency virus (HIV) as the cause of the acquired immunodeficiency syndrome (AIDS) in the 1980s, the HIV epidemic represents the most serious health crisis of our time, a critical and ongoing risk to the health of Americans and populations around the world. In the U.S., more than 1.2 million people are living with HIV infection, and approximately 108 new diagnoses of HIV infection are made daily. More than 36 million people globally live with HIV infection. HIV infection destroys the body's immune system and debilitates its ability to control infections, inflammatory syndromes, and cancer. HIV infection affects people of all ages, gender, and races, and also accelerates the risk of diseases often associated with aging such as heart and neurodegenerative diseases. Investment in HIV/AIDS research to date has led to unprecedented success in the development of diagnostics and multi-drug regimens that can effectively suppress HIV infection and reduce transmission. Additionally, HIV/AIDS research has stimulated significant advances in other related fields such as cancer, hepatitis, neurology, and molecular diagnostics. Unfortunately, despite the scientific advances, there is still no cure for HIV infection, rendering it a chronic disease requiring life-long, daily treatment. Drug-based strategies for the prevention of infection have proven successful, but a vaccine to prevent infection remains elusive. These challenges are reflected in the study of HIV/AIDS both domestically and globally.

HIV/AIDS Research and Translating Findings to Address Emerging Priorities: The U.S. investment in HIV/AIDS research through NIH spans the full spectrum of medical research from basic science to clinical trials, and has led to significant and dramatic advances, which have decreased new infections and saved millions of lives. According to the *HIV Surveillance Report* released by the CDC in 2015, between 2005-2014, the number of new HIV diagnoses in the U.S. declined 19 percent, which may be attributed to prevention efforts based on NIH-funded research. Despite this accomplishment, new infections continue, and by the end of 2014 an estimated 9,731 youth aged 13 to 24 were diagnosed with HIV. That same age group accounted for an estimated 22 percent of all new HIV diagnoses in the U.S., and has caused a change in the

demographics of the epidemic that will last for at least the next 10 years.[1] Inevitably, the youth and growing numbers of other people living with HIV in the U.S. and abroad require treatment for the rest of their lives.

NIH will continue to explore novel ideas and develop basic research discoveries from multiple biomedical and behavioral research fields, build on the scientific advances and knowledge that have been gained, and capitalize on the unique scientific opportunities, to improve the health of those infected with HIV. Through this exploration, NIH intends to aid in successfully developing a safe and effective HIV vaccine, as well as a cure for infection, which will ultimately lead to the end of the HIV/AIDS pandemic.

Priorities for NIH-Funded HIV/AIDS Research: A series of key HIV/AIDS research priorities and cross-cutting research areas that underpin these priorities were developed in 2015 to serve as a guide for the investment in the NIH HIV/AIDS research over the next three to five years.

The overarching priorities for NIH HIV/AIDS research reflected in this Trans-NIH HIV/AIDS research budget request are:

- Vaccine research and other modalities to reduce the incidence of HIV/AIDS
- Next generation of HIV therapies with better safety and ease of use
- Research toward sustained viral remission and develop a cure
- HIV-associated coinfections, comorbidities, and complications

The priority areas are linked by crosscutting areas focused on basic research, research to reduce health disparities, behavior and social science research, and research training.

Enhancing Stewardship within NIH-Funded HIV/AIDS Research: The OAR develops an annual Trans-NIH Plan for HIV-Related Research (Strategic Plan) to ensure that the Trans-NIH AIDS research budget is used to fund the overarching HIV/AIDS research priorities. It provides a roadmap for the NIH HIV/AIDS research effort, which is carried out by nearly all of the NIH Institutes and Centers. The Plan shapes the NIH investment in building on the most recent scientific progress and opportunities to develop a safe and effective AIDS vaccine, generate a cure for HIV/AIDS, and ultimately achieve an end to the AIDS pandemic. The Plan also serves as a resource to inform the public, the scientific community, Congress, and HIV/AIDS-affected communities about the NIH HIV/AIDS research agenda. It is developed through a collaborative process involving broad input from NIH intramural and extramural scientists and other stakeholders.

Starting in FY 2015, the OAR implemented new review processes to align investment of NIH HIV/AIDS dollars with projects in the highest priority areas (overarching priorities) of HIV/AIDS research. These processes include trans-NIH planning, budgeting, and

[1] Centers for Disease Control and Prevention: HIV Among Youth. (2016, April 27). https://www.cdc.gov/hiv/group/age/youth/

encouragement of increased collaboration and partnerships across ICs. NIH developed and implemented a recurring annual comprehensive portfolio review process to assess all grants, contracts, and intramural projects supported with HIV/AIDS funding. As a result of the evaluation processes, OAR has and will continue to allocate and redirect resources across NIH ICs and across the key areas of science to address high research priorities.

Overall Budget Policy:The FY 2018 President's Budget estimate for the trans-NIH AIDS research program is $2,440.180 million, a decrease of $554.178 million compared to the FY 2017 Annualized Continuing Resolution level. The OAR is authorized to allocate all dollars associated with this area of research across the entire NIH. Now that the NIH HIV/AIDS research budget is more tightly focused on high priority HIV/AIDS research, this total amount of funding will support only the highest priority HIV/AIDS research. This includes: 1) discovery, translation, and development of new prevention and treatment modalities for HIV/AIDS including vaccines, monoclonal antibodies, and new drugs, 2) clinical trials to test and develop these new products, 3) enhancing research for achieving a cure or sustained HIV remission , 4) exploring new opportunities for basic scientific research on HIV interactions with cells and the immune responses to the virus and its components and 5) co-morbidities and co-infections associated with HIV/AIDS. In addition, these resource alignment practices have opened opportunities to incorporate improved risk-assessment tools and to enhance better study designs to deliver effective interventions for prevention and treatment of HIV/AIDS.

Program Descriptions and Accomplishments

Vaccine research and reducing the incidence of HIV/AIDS: The best long-term strategy for controlling the HIV/AIDS pandemic is the development of safe, effective, and affordable HIV vaccine(s) that may be used in combination with other prevention strategies. NIH supports a broad research portfolio encompassing basic, preclinical, and clinical research to prevent infection, including studies to identify and understand protective immune responses in HIV-positive individuals and studies of improved animal models for the preclinical evaluation of vaccine candidates. NIH has supported unprecedented collaborative investigations to identify how specific immune responses may protect against HIV acquisition. The OAR is committed to providing resources for the advancement of existing vaccine concepts, as well as supporting innovative basic HIV vaccine research studies that may prevent HIV infection more efficiently than vaccines already tested. New discoveries in HIV vaccine research have radically changed our thinking concerning the design of novel immunogens and strategies to employ them.

A large clinical trial of a promising vaccine candidate, launched in FY 2017 by the HIV Vaccine Trials Network (HVTN) 702, is the first study of its kind in many years and represents the culmination of wide ranging, multidisciplinary efforts to improve upon a vaccine candidate that showed modest success in 2009. In addition to the HVTN 702 study, additional novel HIV vaccine approaches are currently under investigation to maximize the chance for success in this critical field. These approaches include the latest discoveries in human immunology and vaccinology to effect a powerful and long lasting anti-HIV response and to develop antibodies that neutralize HIV. Lastly, these scientific advances are being undergirded by investments in

biologic manufacturing infrastructure to ensure that progress is not impeded by delays in production capacity.

NIH has made dramatic advances in research and development related to HIV prevention in both adults and infants. A recently completed trial ((HIV Prevention Trials Network) HPTN 052) demonstrated that early treatment of HIV-infected individuals to achieve full viral suppression before immune decline resulted in a 93 percent reduction of HIV transmission between sexual partners. Another trial showed that an antiretroviral (ARV)-based intravaginal ring was up to 70 percent effective in preventing sexually-transmitted HIV infection in women who used the ring. In addition, the large Promoting Maternal and Infant Survival Everywhere (PROMISE) trial completed in 2016 demonstrated that HIV positive women, who were treated successfully with ARV during their pregnancy and while breastfeeding, prevented nearly all HIV infections in their infants.

New developments in the HIV prevention field are currently being tested in clinical trials and have the potential to develop safer and more effective prevention strategies. Discoveries by scientists at NIH and elsewhere have led to the development of broadly neutralizing antibodies (bNAbs) that may prevent HIV infection, a concept under evaluation in a pair of trials called "AMP" for Antibody-Mediated Prevention. Another study is evaluating a new injectable drug—Long Acting Cabotegravir—opening the possibility that future prevention modalities will be effective with monthly, rather than daily dosing.

While these breakthroughs are significant and substantial, many challenges remain. For example, prevention products may not be used by individuals on a consistent basis, thereby decreasing their effectiveness. These challenges demonstrate that further research is needed to better understand human behavior and to develop prevention tools and strategies that are effective for all high risk populations.

Next generation of HIV therapies: Antiretroviral (ARV) treatment (ART) has resulted in remarkable immune recovery and physiologic function in HIV-infected individuals who can consistently take prescribed HIV treatment regimens and tolerate occasional side effects or toxicities. Combination ART with several classes of anti-HIV drugs has simplified treatment regimens, delayed the progression of HIV infection to AIDS, prolonged viral suppression, delayed the development of viral resistance, and reduced HIV-associated comorbidity and comortality from other infections (e.g., hepatitis, TB, and pneumonia), chronic diseases, cancers, and neurologic and mental health complications. Despite these treatment advances many challenges remain including: 1) identifying new virus and cell targets to suppress viral replication and to overcome resistance to existing drugs 2) maintaining long-term treatment adherence to keep HIV replication suppressed, thus improving immune competence and prolonging the time to the development of drug resistance, and 3) overcoming the persistent disparities in HIV treatment outcomes across race, gender, and socioeconomic status.

To address the challenges of developing and testing HIV treatments, NIH-funded researchers are engaged in a wide array of research to improve current remedies. Efforts are underway to develop and test HIV treatments that are longer acting, less toxic with fewer side effects and complications, and easier to take, thus improving adherence. In the near future, individuals with

HIV may be able to receive a once monthly injection instead of taking one or more pills every day. Basic and clinical researchers are evaluating therapeutic vaccines that have the potential to effect long term viral remission without the need for additional drugs. Epidemiologists are investigating the spread of drug resistance and strategies to prevent disease progression from one place to another. Behavioral and social scientists are studying novel approaches to get treatment started as soon as an HIV diagnosis is made, as well as how to keep HIV-infected patients in these services to achieve optimal prevention and treatment responses.

Research and develop a cure for HIV/AIDS: The mechanisms by which HIV persists in hidden reservoirs within cells and tissues in the body are not well understood and represents the largest hurdle to finding a cure for HIV. Significant advances to understand the biology of reservoir formation, the ability of a virus to remain dormant within a cell, and viral persistence have been made, but continued research is fundamental to further understand and overcome this barrier. A 2016 breakthrough from NIH researchers showed that some monkeys infected with Simian immunodeficiency virus (SIV)—a virus that is a close relative to HIV—were able to control the virus without continued ART for as long as nine months after a two-step treatment with antiretroviral drugs and a monoclonal antibody that blocks a receptor on immune cells. The mechanism behind this finding is unclear, but research is already initiated to capitalize on this unexpected, seminal breakthrough. Initial human clinical studies to confirm and extend these animal model findings are underway.

In addition, a wide array of basic, preclinical, and clinical research are ongoing to facilitate progress in developing new therapeutic strategies that reliably and reproducibly induce sustained remission of viral replication or viral eradication without antiretroviral treatment (ART). Multiple strategies are in progress in large consortia funded by NIH, including: 1) "kicking" the virus out of its hidden/latent state and "killing" any cells that start producing the virus when ART is not present; 2) creating immune cells that are resistant to HIV infection by manipulating genes so that the virally resistant cells have a survival advantage, and; 3) inducing immune responses that can control HIV.

HIV-associated comorbidities and coinfections: HIV directly and indirectly causes a complex array of health problems that are unresolved by current ART. Immune deficiency and underlying inflammation caused by the virus increases susceptibility to many diseases and amplifies the effects of these diseases. Ongoing basic and observational research continues to shed light on the interaction of HIV with other infections, such as tuberculosis (TB) and hepatitis, and the impact a dysfunctional immune system has on diseases traditionally not regarded as immune-mediated. Critical research on the central nervous system continues to shed light on the impact of HIV infection on cognitive function and neurologic disorders.

These findings are actively being translated into clinical trials of new drugs and diagnostics so as to accelerate improvement in the health outcomes of people living with HIV/AIDS. NIH is currently funding a host of trials evaluating drugs to prevent and/or treat heart disease, TB disease, hepatitis and other opportunistic infections, underlying inflammation, and neurologic complications.

Crosscutting Areas
A major proportion of HIV/AIDS research has relevance to not one, but all of the overarching NIH HIV/AIDS priority research areas. This includes basic research, health disparities research, behavior and social sciences research, training and capacity building, and information dissemination.

- **Basic Research**: Major gaps remain in our understanding of the basic biology of HIV transmission and pathogenesis; development of immune dysfunction and chronic inflammation; host microbiome, genetic determinants and innate immunity that may either prevent or accelerate disease; and other fundamental issues that underpin the development of high-priority strategies for the prevention, treatment, and cure of HIV and related co-morbidities and coinfections.

- **Epidemiological Research**: The lifetime risk of being diagnosed with HIV in the U.S. is greater for people living in the South, including the District of Columbia, than in other regions of the country.[2] Understanding causes, patterns, and social phenomenon that have led to higher rates of HIV infection in the South and Midwest of the U.S. is key to rapidly identifying and preventing HIV outbreaks such as the one that recently occurred in Indiana. With a surging opioid epidemic, particularly in youth in the U.S., methodology to detect infection clusters early and prevent future outbreaks has become a cross-cutting and cross-discipline priority.

- **Behavioral and Social Science Research:** HIV/AIDS-related behavioral and social science research is integrated within all of the high-level priorities for HIV/AIDS research including prevention and treatment of HIV infection, developing a cure, and research on comorbidities and co-infections. Behavioral and social science research findings continue to reveal a wide range of individual, interpersonal, social, structural, and other factors that contribute to and drive the HIV/AIDS pandemic.

- **Research to Reduce Health Disparities:** The disproportionate rate of infections in racial and ethnic minorities, especially young men who have sex with men (MSM) of color, as well as the disturbing trends in treatment outcomes of those living with HIV/AIDS, supports the ongoing research funding to discover ways to resolve these disparities. Defining where the gaps occur and the immediate causes will go a long way to addressing biologic, genetic, epidemiologic risk and behavioral differences that can systematically be addressed to change the course of HIV infection in these populations.

- **Training, Infrastructure, and Capacity Building:** Training of the biomedical, behavioral, and social science workforce required to conduct high-priority HIV/AIDS research has long been a goal of the OAR office. NIH provides support for infrastructure

[2] Centers for Disease Control and Prevention: HIV Surveillance Report, 2015; vol. 27, published November 2016. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html.

and capacity building as integral components of its commitment to carry out highly productive HIV-related research that is both scientifically and ethically sound. 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 HIV/AIDS research.

- **Information Dissemination:** NIH supports innovative initiatives to enhance the dissemination of research findings. The diversity of communities makes it imperative that dissemination approaches address the different levels of scientific literacy and how information is accessed. Tailoring the scientific information for each community is a priority. NIH research findings are used to develop state-of-the-art U.S. HIV/AIDS treatment and prevention guidelines. The OAR coordinates the development, update, and distribution of U.S. guidelines for HIV/AIDS treatment. The need to effectively and rapidly translate HIV/AIDS research into practice requires new and innovative approaches to reach diverse stakeholders including research investigators, health providers, policy makers, the public, and HIV-infected and -affected individuals.

Benefits of AIDS Research to Other Areas: NIH investment in HIV/AIDS research has resulted in critical scientific accomplishments that benefit not only the nearly 37 million HIV-positive individuals around the world, but also has contributed knowledge to the prevention, diagnosis, and treatment of many other diseases and conditions. HIV/AIDS research has driven the overall understanding of immunology, virology, microbiology, molecular biology, and the impact of genetics on human health. 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, comorbidities, cancers, and other complications.

HIV/AIDS research continues to make discoveries that can be applied to other infections and conditions such as cancer, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia. HIV research initially benefitted from prior NIH-funded research on viruses that cause cancer, and now paves the way with new areas of basic research that applies to other diseases and conditions. Some of the benefits and discoveries as a result of HIV/AIDS research include:

- HIV/AIDS research has advanced the understanding of the relationships between viruses, immune regulation, and cancer.
- HIV/AIDS research has directly led to new treatments for cancer that transform a patient's immune system to fight the cancer directly.
- Research on HIV-associated neurologic and cognitive manifestations similarly may benefit millions of individuals 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 B and hepatitis C infections, which currently affect more than 185 million people globally, has been revolutionized and curative regimens are now

available because of the development of specific drugs that directly interfere with virus replication.

- Blood supplies are safe from multiple infectious disease agents, because of nucleic acid tests and test concepts that were developed, refined, and implemented to prevent HIV-contaminated blood from being used for transfusions.
- HIV/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.

Conclusion: The NIH investment in HIV/AIDS research continues to produce significant groundbreaking scientific advances, unprecedented scientific opportunities, as well as new challenges. NIH's leadership and commitment to build on these advances and strategically allocate funds to the highest priorities are essential to successfully develop a safe and effective HIV/AIDS vaccine, reduce the incidence of new infections, develop strategies for sustained viral remission, and ultimately bring an end to the HIV pandemic.