DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research Trans-NIH AIDS Research Budget

# OAR Office of the Director

**Director:** *Dr. Jack Whitescarver*

**Senior Advisor:** *Ms. Wendy Wertheimer*

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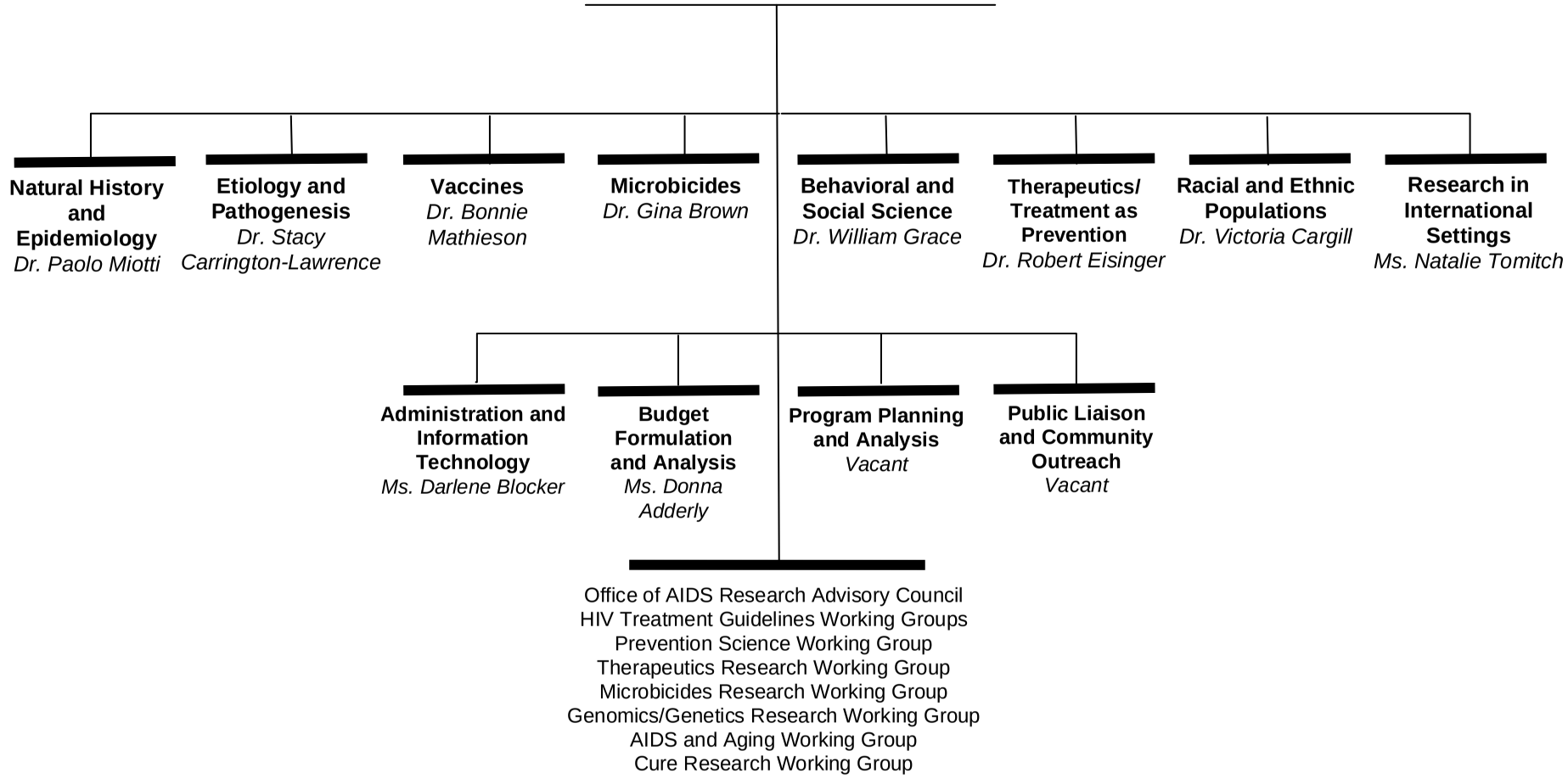
*Dr. Robert Eisinger*




Office of AIDS Research Advisory Council
HIV Treatment Guidelines Working Groups
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

**NATIONAL INSTITUTES OF HEALTH**
**Office of AIDS Research**
**Budget Authority by Institute and Center**

| Institute/ Center | FY 2011 Actual | FY 2012 Enacted | FY 2013 President's Budget | Change |
|---|---|---|---|---|
| NCI | $269,953,000 | $271,692,000 | $272,003,000 | $311,000 |
| NHLBI | 67,606,000 | 67,995,000 | 68,355,000 | 360,000 |
| NIDCR | 20,049,000 | 20,061,000 | 19,112,000 | (949,000) |
| NIDDK | 30,752,000 | 30,951,000 | 27,635,000 | (3,316,000) |
| NINDS | 46,557,000 | 46,857,000 | 46,614,000 | (243,000) |
| NIAID | 1,563,349,000 | 1,572,973,000 | 1,580,784,000 | 7,811,000 |
| NIGMS | 64,785,000 | 65,202,000 | 65,548,000 | 346,000 |
| NICHD | 144,370,000 | 144,924,000 | 145,792,000 | 868,000 |
| NEI | 10,537,000 | 8,902,000 | 784,000 | (8,118,000) |
| NIEHS | 5,304,000 | 5,338,000 | 5,338,000 | - |
| NIA | 5,596,000 | 5,632,000 | 5,632,000 | - |
| NIAMS | 4,894,000 | 4,925,000 | 5,425,000 | 500,000 |
| NIDCD | 1,865,000 | 1,877,000 | 1,877,000 | - |
| NIMH | 189,347,000 | 190,513,000 | 190,513,000 | - |
| NIDA | 317,348,000 | 319,292,000 | 321,163,000 | 1,871,000 |
| NIAAA | 28,200,000 | 28,380,000 | 28,848,000 | 468,000 |
| NINR | 12,561,000 | 12,642,000 | 12,642,000 | - |
| NHGRI | 7,085,000 | 7,130,000 | 7,279,000 | 149,000 |
| NIBIB | 2,774,000 | 3,699,000 | 3,329,000 | (370,000) |
| NIMHD | 20,316,000 | 20,446,000 | 20,573,000 | 127,000 |
| NCCAM | 2,441,000 | 1,610,000 | 1,610,000 | - |
| NCATS | 67,910,000 | 68,328,000 | 68,328,000 | - |
| FIC | 24,086,000 | 24,241,000 | 24,426,000 | 185,000 |
| NLM | 7,616,000 | 7,665,000 | 7,665,000 | - |
| OD | | | | |
| OAR | 63,302,000 | 63,802,000 | 63,802,000 | - |
| ORIP | 80,674,000 | 79,844,000 | 79,844,000 | - |
| Subtotal | 143,976,000 | 143,646,000 | 143,646,000 | - |
| TOTAL, NIH | $3,059,277,000 | $3,074,921,000 | $3,074,921,000 | - |

## NATIONAL INSTITUTES OF HEALTH

### Budget Authority by Mechanism - AIDS [1]

(Dollars in Thousands)

| MECHANISM | FY 2011 Actual [3] | | FY 2012 Enacted [4] | | FY 2013 PB | | Change | |
|---|---|---|---|---|---|---|---|---|
| | No. | Amount | No. | Amount | No. | Amount | No. | Amount |
| Research Grants: | | | | | | | | |
| Research Projects: | | | | | | | | |
| Noncompeting | 1,784 | $1,353,726 | 1,691 | $1,318,106 | 1,675 | $1,141,964 | (16) | ($176,142) |
| Administrative Supplements | *76* | 8,015 | *50* | 7,760 | *48* | 6,205 | (2) | (1,555) |
| Competing | 559 | 295,891 | 646 | 322,489 | 677 | 481,564 | 31 | $159,075 |
| Subtotal, RPGs | 2,343 | $1,657,632 | 2,337 | $1,648,355 | 2,352 | $1,629,733 | 15 | ($18,622) |
| SBIR/STTR | 71 | $35,243 | 74 | $38,064 | 80 | $43,138 | 6 | 5,074 |
| Research Project Grants | 2,414 | $1,692,875 | 2,411 | $1,686,419 | 2,432 | $1,672,871 | 21 | ($13,548) |
| Research Centers: | | | | | | | | |
| Specialized/Comprehensive | 73 | $135,074 | 82 | $141,928 | 80 | $140,403 | (2) | ($1,525) |
| Clinical Research | 1 | 55,801 | 1 | 56,199 | 1 | 56,199 | 0 | 0 |
| Biotechnology | 0 | 4,778 | 0 | 4,668 | 0 | 4,692 | 0 | 24 |
| Comparative Medicine | 12 | 57,257 | 9 | 55,332 | 10 | 56,765 | 1 | 1,433 |
| Research Centers in Minority Institutions | 3 | 14,475 | 3 | 14,564 | 3 | 14,566 | 0 | 2 |
| Research Centers | 89 | $267,385 | 95 | $272,691 | 94 | $272,625 | (1) | ($66) |
| Other Research: | | | | | | | | |
| Research Careers | 240 | $42,565 | 242 | $43,304 | 228 | $41,720 | (14) | ($1,584) |
| Cancer Education | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cooperative Clinical Research | 12 | 17,309 | 12 | 17,515 | 9 | 10,464 | (3) | (7,051) |
| Biomedical Research Support | 2 | 1,873 | 3 | 2,809 | 3 | 2,809 | 0 | 0 |
| Minority Biomedical Research Support | 2 | 503 | 2 | 503 | 2 | 505 | 0 | 2 |
| Other | 140 | 62,894 | 132 | 61,664 | 136 | 64,668 | 4 | 3,004 |
| Other Research | 396 | $125,144 | 391 | $125,795 | 378 | $120,166 | (13) | ($5,629) |
| Total Research Grants | 2,899 | $2,085,404 | 2,897 | $2,084,905 | 2,904 | 2,065,662 | 7 | (19,243) |
| Research Training: | FTTPs | | FTTPs | | FTTPs | | | |
| Individual Awards | 84 | $3,384 | 73 | $3,275 | 74 | $3,452 | 1 | $177 |
| Institutional Awards | 669 | 33,159 | 661 | 33,606 | 648 | 33,446 | *(13)* | *($160)* |
| Total Research Training | 753 | $36,543 | 734 | $36,881 | 722 | $36,898 | (12) | $17 |
| | | | | | | | FTEs | |
| Research & Development Contracts | 133 | $410,523 | 130 | $427,710 | 122 | $447,838 | (8) | $20,128 |
| *(SBIR/STTR)* | *1* | *$654* | *1* | *$654* | *1* | *$654* | *0* | *$0* |
| | FTEs | | FTEs | | FTEs | | | 0 |
| Intramural Research | | $338,877 | | $336,945 | | $336,197 | 0 | (748) |
| Research Management and Support | | 124,628 | | 124,678 | | 124,524 | 0 | (154) |
| *Office of the Director - Appropriation* | | *$143,976* | | *$143,646* | | *$143,646* | | *($0)* |
| Office of the Director - Other [2] | | 63,302 | | 63,802 | | 63,802 | | 0 |
| *ORIP & SEPA [2]* | | *80,674* | | *79,844* | | *79,844* | | (0) |
| **Total, NIH Discretionary B.A.** | | **$3,059,277** | | **$3,074,921** | | **$3,074,921** | | **$0** |

[1] All items in italics are "non-adds"; items in parenthesis are subtractions.

[2] Number of grants and dollars for the Common Fund, ORIP and SEPA components of OD are distributed by mechanism and are noted here as a non-add. ORIP and SEPA established consistent with NCATS reorganization.

[3] Reflects NCATS reorganization.

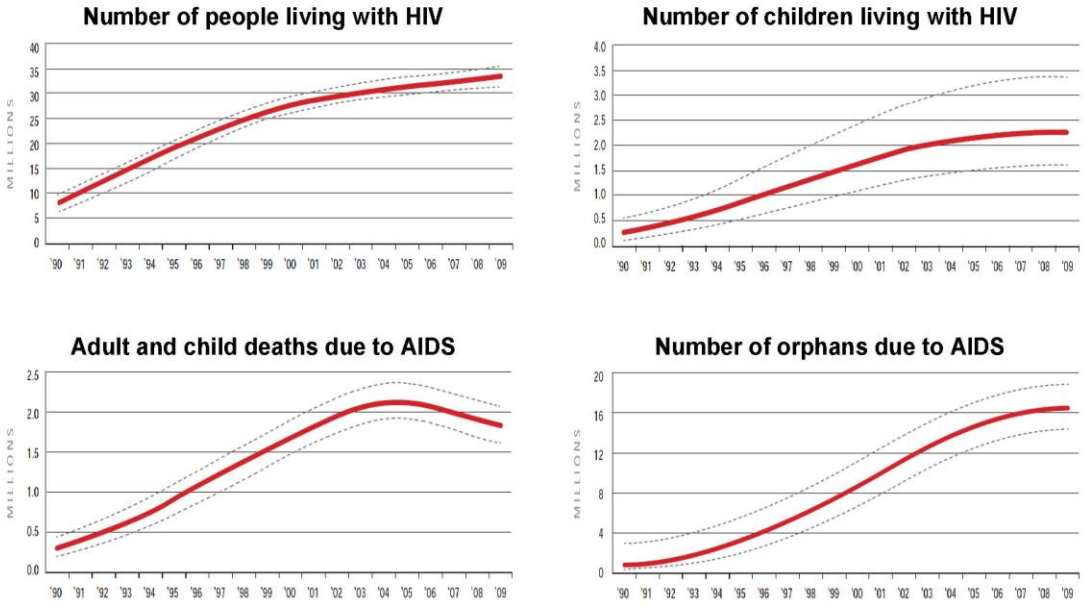
[4] Reflects AIDS component of Secretary's Transfer of $8.7M.

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

| Area of Emphasis | FY 2009 Actual | FY 2010 Actual | FY 2011 Actual | FY 2012 Enacted | FY 2013 Pres. Bud. | Dollar Change |
|---|---|---|---|---|---|---|
| HIV Microbicides | $128,670 | $143,162 | $120,982 | $127,673 | $130,226 | $2,553 |
| Vaccines | 560,956 | 534,972 | 548,834 | 549,593 | 560,585 | 10,992 |
| Behavioral and Social Science | 434,305 | 429,313 | 412,163 | 424,115 | 428,356 | 4,241 |
| Therapeutics | | | | | | |
| *Therapeutics as Prevention* | *84,775* | *67,734* | *65,064* | *75,874* | *76,068* | |
| *Drug Discovery, Development, and Treatment* | *585,786* | *617,257* | *615,475* | *620,491* | *604,281* | |
| Total, Therapeutics | 670,561 | 684,991 | 680,539 | 696,365 | 680,349 | (16,016) |
| Etiology and Pathogenesis | 729,991 | 744,649 | 730,978 | 723,245 | 731,322 | 8,077 |
| Natural History and Epidemiology | 247,914 | 275,098 | 278,998 | 282,235 | 276,599 | (5,636) |
| Training, Infrastructure, and Capacity Building | 198,028 | 216,329 | 232,624 | 221,817 | 217,606 | (4,211) |
| Information Dissemination | 48,868 | 56,832 | 54,159 | 49,878 | 49,878 | - |
| Total | $3,019,293 | $3,085,346 | $3,059,277 | $3,074,921 | $3,074,921 | - |

Figure 2.5

## Global HIV trends, 1990 to 2009




Dotted lines represent ranges, solid lines represent the best estimate.

*Source:* UNAIDS.

**Justification of Budget Request**
**OFFICE OF AIDS RESEARCH**
***Trans-NIH AIDS Research Budget Justification***

Budget Authority (BA):

| FY 2011 Actual | FY 2012 Enacted | FY 2013 President's Budget | FY 2013+/- FY 2012 |
|---|---|---|---|
| $3,059,277,000 | $3,074,921,000 | $3,074,921,000 | --- |

## DIRECTOR'S OVERVIEW

***30 Years of Extraordinary NIH AIDS Research Accomplishments:*** HIV, the virus that causes AIDS, is one of the most complex pathogens to affect human health and challenge biomedical research. In the three decades since AIDS was first recognized, NIH has established the world's leading AIDS research program. This investment in HIV research has transformed the disease from a mysterious and uniformly fatal infection into one that can be accurately diagnosed and effectively managed with appropriate treatment. A recent study estimated that **14.4 million life-years have been gained among adults around the world since 1995 as a result of AIDS therapies developed through NIH-funded research.**[1] NIH research has resulted in landmark advances that have led to:

- co-discovery of HIV, the virus that causes AIDS;
- development of the first blood test for the disease, which has allowed diagnosis of infection as well as ensured the safety of the blood supply;
- the critical discovery of key targets to develop antiretroviral therapies (ART) and multi-drug regimens that have resulted in improved life expectancy for those with access to and who can tolerate these drugs; and the development of treatments for many HIV-associated coinfections, comorbidities, malignancies, and clinical manifestations, with benefits for patients also suffering from those other diseases;
- groundbreaking strategies for the prevention of mother-to-child transmission, which have resulted in dramatic decreases in perinatal HIV in the United States;
- demonstration that the use of male circumcision can reduce the risk of HIV acquisition;
- the first step in proving the concept that a vaccine to prevent HIV infection is feasible; and discovery of two potent human antibodies that can stop more than 90 percent of known global HIV strains from infecting human cells in the laboratory;
- demonstration of the first proof of concept for the feasibility of a microbicide gel capable of preventing HIV transmission;
- demonstration that the use of therapy by infected individuals can dramatically reduce transmission to an uninfected partner;

[1] Sexually Transmitted Infections. 2010 Dec; 86 Suppl 2:ii67-71.

- demonstration of the potential feasibility of pre-exposure prophylaxis (PrEP), that long-term use of antiretroviral treatment regimens by some groups of high-risk uninfected individuals can reduce risk of HIV acquisition;
- discovery that genetic variants may play a role in protecting some individuals, known as "elite controllers," who have been exposed to HIV over an extended period, from developing symptoms and enabling them to control the infection without therapy;
- critical basic science discoveries that continue to provide the foundation for novel research; and
- progress in both basic and treatment research efforts aimed at eliminating viral reservoirs in the body, which is, for the first time, leading scientists to design and conduct research aimed at a cure.

***The Pandemic:*** Despite considerable progress in the past year, the HIV/AIDS epidemic continues to expand. UNAIDS estimates that in 2010, more than 34 million people were living with HIV/AIDS; 2.7 million were newly infected; and 1.8 million people died of AIDS-related illnesses. In the United States, CDC estimates that more than 1.2 million people are HIV-infected; and someone is infected with HIV every 9-and-a-half minutes. AIDS disproportionately affects racial and ethnic populations, women of color, young adults, and men who have sex with men. The AIDS pandemic has devastating consequences around the world in virtually every sector of society. Further research to improve prevention and treatment is urgently needed. Advances in prevention and treatment also will have extensive economic benefits.

***Mission:*** The Office of AIDS Research (OAR) coordinates the scientific, budgetary, and policy elements of the trans-NIH research program on AIDS and its wide spectrum of associated malignancies, coinfections, and clinical complications. OAR functions as an "institute without walls" with responsibility for AIDS-related research supported by every NIH Institute and Center (IC). Through its unique trans-NIH processes, OAR identifies the highest priority areas of scientific opportunity, enhances collaboration, minimizes duplication, and ensures that precious research dollars are invested effectively. The OAR identifies trans-NIH AIDS research program priorities and shifts resources across ICs and areas of science as needed to meet the changing epidemic and scientific opportunities.

***Extraordinary Opportunities for FY 2013:*** Secretary of State Hillary Clinton stated that scientific advances have created a "historical opportunity" to change the course of the pandemic and usher in the possibility of an AIDS-free generation, a goal that would have been previously unimaginable. Advances made by NIH investigators have opened doors for new and exciting research opportunities to answer key scientific questions that remain in the search for strategies to prevent and treat HIV infection both in the United States and around the world, and represent the building blocks for the development of this trans-NIH AIDS research budget:

- **Investing in Basic Research:** OAR will increase support for basic research that will underpin further development of critically needed ***vaccines and microbicides.***
- **Encouraging New Investigators and New Ideas:** OAR will provide additional support for innovative multidisciplinary research and international collaborations to develop novel approaches and strategies to eliminate viral reservoirs that could lead toward ***a cure for HIV***.

- **Accelerating Discovery Through Technology:** OAR will increase funds to support critical studies in the area of ***therapeutics as a method to prevent infection***, including treatment to prevent HIV infection after exposure; pre-exposure prophylaxis (PrEP); a potential prevention strategy known as "test and treat," to determine whether a community-wide testing program with treatment can decrease the overall rate of new HIV infections; and improved strategies to prevent mother-to-child transmission. A key priority is to evaluate prevention interventions that can be used in combination in different populations, including adolescents and older individuals.
- **Improving Disease Outcomes:** OAR will target funding for NIH research focused on developing better, less toxic treatments and investigating how genetic determinants, sex, gender, race, age, nutritional status, treatment during pregnancy, and other factors interact to affect treatment success or failure and/or disease progression. Studies will address the increased incidence of malignancies, cardiovascular and metabolic complications, and premature aging associated with long-term HIV disease and ART.
- **Advancing Translational Sciences:** OAR will ensure adequate resources for research on the feasibility, effectiveness, and sustainability required to scale-up interventions from a structured behavioral or clinical study to a broader "real world" setting.

**Overall Budget Policy:** To address these priorities, the OAR FY 2013 President's Budget request for the trans-NIH AIDS research program is $3,074.921 million, which is the same amount as the FY 2012 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, coinfections, and clinical complications; as well as research management support; research centers; and training. OAR has provided increases to high-priority prevention research in the areas of microbicides, vaccines, behavioral and social science, and treatment as prevention research, as well as to etiology and pathogenesis research that provides the essential basic science foundation not only for AIDS-related research but for other related diseases and conditions as well. In order to provide those increases, OAR has reduced and redirected funds from natural history and epidemiology, therapeutics, and training and infrastructure support.

## PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

***Trans-NIH Strategic Plan and Budget:*** OAR's trans-NIH planning process, involving both government and non-government experts, and representatives from community constituency groups results in the identification of overarching AIDS-research priorities and specific research objectives and strategies. OAR develops each IC's AIDS allocation based not on a formula, but on the scientific priorities and objectives of the annual trans-NIH AIDS research strategic plan, taking into account the current scientific opportunities 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 may be the best hope for woman-controlled HIV prevention. Microbicides are antimicrobial agents and other products that could be applied topically and used alone or in combination with other strategies to prevent transmission of HIV and other sexually transmitted infections. Microbicides represent a promising approach to primary prevention. 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 aimed at understanding how HIV crosses mucosal membranes and infects cells; behavioral and social science research on adherence to, acceptability of, and use of microbicides among different populations; studies of 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 testing different ARV- and non-ARV-based products are under way or being developed.

**Budget Policy:** The FY 2013 President's Budget request for Microbicides is $130.226 million, which represents an increase of $2.553 million and 2.0 percent over the FY 2012 enacted level for this high-priority area of research. In FY 2013, NIH will continue to support the discovery, design, development, and evaluation of microbicide candidates. Key ongoing activities include support for the microbicide clinical trials network and the necessary infrastructure to conduct microbicide trials. Research activities will be designed to build on recent research advances; develop innovative, novel, and high risk-high reward approaches for the discovery, development and testing of microbicide candidates and microbicide delivery systems; develop criteria for selecting products to be advanced through the different phases of preclinical and clinical studies, including clinical effectiveness studies; and research on ethics, adherence, and other behavioral and social science issues that can affect clinical trials and product 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 announcement of the results of the RV144 trial in Thailand, NIH has supported an unprecedented collaborative effort with investigators around the world to identify clues about the necessary immune responses required to protect against HIV acquisition. To take advantage of the knowledge gained, it now will be essential to conduct additional clinical trials in other populations and in other parts of the world. The recent release of data from this and several vaccine Phase I and Phase II clinical studies presents new scientific opportunities for investigation.

**Budget Policy:** The FY 2013 President's Budget request for Vaccines is $560.585 million, an increase of $10.992 million and 2.0 percent over the FY 2012 enacted level. Basic research studies, particularly those using samples from ongoing clinical trials, are critically needed on the virus and host immune responses that can inform the development of new and innovative vaccine concepts, as well as the development of improved animal models to conduct preclinical evaluations of vaccine candidates. In FY 2013, NIH will fund additional basic research in these areas, as well as the design and development of new vaccine concepts and the preclinical/clinical development of vaccine candidates in the pipeline. Resources will be directed toward the development and testing of improved vaccine candidates in additional clinical studies, both in the United States and abroad, building on the results of the recent Phase III vaccine trial in Thailand. This also includes support for new initiatives to integrate systems biology with HIV vaccine discovery and for additional research involving nonhuman primates. These initiatives will build on the partial protection and newly identified markers that may be related to the early protection observed in the trial conducted in Thailand and will develop new test systems to measure immune responses to the vaccine that will integrate preclinical animal and human clinical studies. 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

NIH supports research to better understand the risk behaviors and social contexts that lead to HIV infection and disease progression, how to change those behavioral and social contexts, and how to maintain protective behaviors once they are adopted. Studies are developing and evaluating interventions directly targeted to substance abuse and sexual behaviors associated with HIV transmission. Social and environmental factors associated with infection and disease outcomes are being studied, including housing, employment, health care access, stigma, and interpersonal networks. An important area of research is determining effective strategies to test HIV-infected persons, link them to care, and promote adherence to antiretroviral therapy. Studies have shown that early access to medical care substantially reduces direct medical treatment expenditures. Early linkage to care has been shown to extend life expectancy and can result in health care cost savings. Comprehensive approaches that integrate biomedical and behavioral science perspectives are necessary to develop the needed range of preventive and therapeutic strategies. NIH also supports research to improve methodologies for the conduct of

behavioral studies and related investigations, including ways to improve recruitment into clinical trials, to enhance statistical analysis of behaviors such as alcohol use that can affect medication studies, and to characterize behavioral traits relevant to genetic or genomic studies.

**Budget Policy:** The FY 2013 President's Budget request for Behavioral and Social Science is $428.356 million, which is an increase of $4.241 million and 1.0 percent above the FY 2012 enacted level. NIH will continue to fund research to reduce HIV-related risk behaviors and to better understand social factors contributing to HIV transmission, with an emphasis on racial and ethnic communities most affected by HIV. Resources will be directed toward several new prevention initiatives, addressing the challenges of integrating behavioral and social science methods with biomedical prevention strategies, community-based approaches to engaging and retaining persons in care, and the impact of improved care on reducing HIV transmission. 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. Groundbreaking strides have been made toward 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 and affect treatment success or failure, including immune dysregulation and inflammation, and the development of HIV-associated comorbidities, malignancies, coinfections (including TB and hepatitis C), and cardiovascular, neurological, and other clinical complications. Additional research examining the genetic determinants associated with HIV susceptibility, disease progression, and treatment response is also needed and may lead to the development of customized therapeutic and preventive regimens formulated for an individual patient based on his or her genetic sequence. A gene sequence associated with adverse reactions to the drug abacavir and genes associated with susceptibility to HIV infection in a small subset of individuals already have been identified. Research examining the mechanisms by which HIV establishes and reactivates latent reservoirs of infection, and studies that further understanding of factors that are associated with the ability of the host to restrict HIV infection and/or mitigate HIV disease progression is also a high priority for NIH. A better understanding of these processes could help identify key targets for the development of new therapeutic strategies to prevent or control HIV infection or possibly lead to a cure for HIV disease.

**Budget Policy:** The FY 2013 President's Budget request for Etiology and Pathogenesis is $731.322 million, which is an increase of $8.077 million and 1.12 percent over the FY 2012 enacted level. The results from recent microbicide, vaccine, and pre-exposure prophylaxis (PrEP) clinical studies have revealed gaps in knowledge and understanding of HIV etiology and pathogenesis, particularly with regard to host immune responses, how HIV interacts with and transverses mucosal surfaces, and the establishment and maintenance of latent viral reservoirs. NIH will provide increased resources for research on the biology of HIV transmission, which will be of importance for all HIV prevention research. An important new area will focus on issues related to the potential for a cure or lifelong remission of HIV infection, including studies on viral persistence, latency, immune activation, and inflammation. Basic research to better understand HIV coinfections, comorbidities and malignancies, as well as factors related to premature aging and other complications will be priorities. Funds also will be provided for research to better understand the differences in HIV transmission, treatment, and progression in women compared with men as well as the unique clinical manifestations of HIV disease in women.

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## THERAPEUTICS

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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 has also 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 developing drug resistance. Recent epidemiologic studies have shown that the incidence of coinfections, comorbidities, 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 drugs to maintain undetectable viral load, to overcome drug resistance and treatment failure, and to prevent and treat HIV-associated coinfections, comorbidities, and other complications. The program is also focused on developing drugs and other strategies that can eradicate persistent viral reservoirs that may lead to a functional cure for HIV disease.

**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 (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 (iPrEx) demonstrated that 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). However, these findings have not been replicated in women. Additional strategies currently being investigated include: PrEP in high-risk uninfected women and adolescents; post-exposure prophylaxis; the use of treatment to prevent HIV infection after accidental exposure, including in a health care environment; and 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 2013 President's Budget request for Therapeutics is $680.349 million, which represents a decrease of $16.016 million and 2.3 percent below the FY 2012 enacted level. The overall funding for therapeutics research will be reduced to allow for increased funding for HIV prevention science research, including the development and clinical testing of potential microbicides, vaccines, and behavioral and social science interventions. A portion of the funds from expiring grants and contracts for therapeutics research will be reallocated to studies on the treatment and prevention of HIV-associated coinfections and comorbidities and to support crucial basic research on HIV and genomics studies on the host immune response to HIV. Resources within the area of Therapeutics also will be directed to support: the recompetition of the Leadership Groups for the NIH Clinical Trials Research Networks; several new and/or expanded initiatives to develop innovative therapies and novel cell- 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; and delineating the interaction of aging and neuro-AIDS. Increased funding will be provided for the area of *Therapeutics as Prevention,* including discovery and testing the next generation of antiretroviral drugs that may be used in potential new strategies for PrEP (therapeutic regimens for uninfected at-risk individuals); treatment of infected individuals to prevent transmission; post-exposure prevention; and new regimens to prevent mother-to-child transmission.

## NATURAL HISTORY AND EPIDEMIOLOGY

Natural history and epidemiologic research on HIV/AIDS is critical to the monitoring of epidemic trends, the evaluation of prevention modalities, the characterization of the clinical manifestations of HIV disease and related comorbidities, and the measurement of the effects of treatment regimens at the population level. Multi-site epidemiologic studies in the United States are identifying new HIV-related comorbidities and helping to differentiate effects related to HIV treatment from those related to HIV disease itself. As the AIDS epidemic evolves, 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 coinfections; malignancies; and 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; within younger and older age groups; and health disparities based on sexual identity).

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 2013 President's Budget request for Natural History and Epidemiology is $276.599 million, which represents a decrease of $5.636 million and 2.0 percent below the FY 2012 enacted level. NIH will continue to provide support for high-priority epidemiology studies of groups and populations affected by HIV and at high risk of infection, including individuals over 50 years of age; men who have sex with men (MSM), especially MSM of color; women; and adolescents. NIH also will increase support for critical studies of the specific role of race and gender, the effects of increased HIV testing and linkage to care on HIV spread, the impact of therapy in changing the spectrum of HIV disease, and the preventable causes of death. In addition, resources will be provided for studies of HIV in aging populations and for implementation science, including how to implement strategies to scale up cost-effective interventions that might accelerate the progress toward an AIDS-free generation.

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## TRAINING, INFRASTRUCTURE, AND CAPACITY BUILDING

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NIH supports the training of domestic and international biomedical and behavioral AIDS researchers, and provides infrastructure, equipment, shared instrumentation, tissue and specimen repositories, and capacity-building support for the conduct of AIDS-related research, including preclinical and clinical studies. The expansion of NIH-funded HIV research globally has necessitated the development of research training, infrastructure, and capacity-building efforts in many resource-limited settings throughout the world. NIH-funded programs have increased the number of training positions for AIDS-related researchers, including programs specifically designed to recruit individuals from underrepresented populations into research careers and to build research infrastructure at minority-serving institutions in the United States. These efforts are integral to strengthening the quality and the reach of HIV/AIDS research, both domestically and internationally.

**Budget Policy:** The FY 2013 President's Budget request for Training, Infrastructure, and Capacity Building is $217.606 million, which represents a decrease of $4.211 million and 1.9 percent below the FY 2012 enacted level. NIH will support training programs for United States and international researchers to build the critical capacity to conduct AIDS research both in racial and ethnic communities in the United States and in developing countries. NIH will continue to support ongoing efforts to increase the supply of nonhuman primates and other animal models, particularly rhesus macaques, for AIDS research and other areas of biomedical research both in the United States and abroad. Support also will be provided for the NIH AIDS Research Loan Repayment Program and the Intramural AIDS Research Fellowship Program that will help ensure an adequate number of trained AIDS researchers at NIH.

## INFORMATION DISSEMINATION

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 United States 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. 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.

**Budget Policy:** The FY 2013 President's Budget request for Information Dissemination is $49.878 million, which is the same amount as the FY 2012 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. In addition, funding 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, will be updated regularly and disseminated widely to health care providers and patients through the AIDS*info* 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 United States. These research programs also enhance research infrastructure, and training of in-country scientists and health care 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 or medical institutions.

**AIDS Research Conducted in International Settings**
(Dollars in millions)

| FY 2011 Actual | FY 2012 Enacted | FY 2013 PB |
|---|---|---|
| **$375.733** | **$364.455** | **$388.862** |

## THE NATIONAL HIV/AIDS STRATEGY

In July 2010, the Administration released the first comprehensive *National HIV/AIDS Strategy (NHAS)* for the United States. Senior officials from NIH are involved in the Federal interagency working group that continues to work with the White House to implement the NHAS. The National Strategy focuses on reducing the number of new HIV infections; increasing access to care for people living with HIV and improving disease outcomes; reducing HIV-related health disparities; and achieving a more coordinated national response. With the authority to direct and coordinate resources for HIV/AIDS research across NIH, OAR has a critical role to play in ensuring that NIH funding for domestic HIV/AIDS research focuses on projects that support the goals of the NHAS.

## BENEFITS OF AIDS RESEARCH TO OTHER AREAS OF RESEARCH

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 because of 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, comorbidities, 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 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.