DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

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JUSTIFICATION
OFFICE OF AIDS RESEARCH

Budget Authority:

	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Budget Authority	$2,849,952,000	$2,920,551,000	$2,932,992,000	$12,441,000

INTRODUCTION

The Global HIV/AIDS Pandemic

Group	**People Newly Infected in 2004**	**People Living with HIV/AIDS in 2004**	**AIDS Deaths in 2004**
Adults *Women*	4.3 million	37.2 million *17.6 million*	2.6 million
Children	640,000	2.2 million	510,000
Total *Source: UNAIDS*	4.9 million	39.4 million	3.1 million

The impact of the global HIV pandemic is profound, affecting families, agriculture and famine, business, healthcare, education, and national economic growth. It is the deadliest epidemic of our generation. The United Nations General Assembly's Declaration of Commitment on HIV/AIDS states "...the global HIV/AIDS epidemic, through its devastating scale and impact, constitutes a global emergency and one of the most formidable challenges to human life and dignity, as well as to the effective enjoyment of human rights, which undermines social and economic development throughout the world and affects all levels of society—national, community, family, and individual."[1] The AIDS epidemic will continue to have devastating consequences around the world for decades to come for virtually every sector of society.

A new United Nations report states: "The disease has such a staggering impact because it weakens and kills many people in their young adulthood, the most productive years for income generation and family caregiving. It destroys families, eliminating a whole generation crucial for the survival of the younger and older persons in society."[2] A recent article stated that: "The spread of HIV/AIDS through Eurasia, in short, will assuredly qualify as a humanitarian tragedy—but it will be much more than that. The pandemic there stands to affect, and alter, the economic potential—and by extension, the military power—of the region's major states...Over the decades ahead, in other words, HIV/AIDS is set to be a factor in the very balance of power within

[1] The Impact of AIDS" (Department of Economic and Social Affairs, United Nations, 2004).

[2] Ibid.

Eurasia—and thus in the relationship between Eurasian states and the rest of the world."[3] Dramatic increases in HIV infection also are occurring in Eastern Europe, Central Asia, Latin America, and the Caribbean.

HIV/AIDS GLOBAL CRISIS

Reversing 3 decades of development gains
National security issue
Economic decline of 10-40%
Health system chaos
Political and military instability
Famine
Rapidly increasing number of orphans
Immense humanitarian concerns

HIV has already infected more than 60 million people around the world, and AIDS has surpassed tuberculosis and malaria as the leading infectious cause of death worldwide.[4] Curbing the transmission of HIV from infected mother to infant is an especially compelling challenge in resource-poor countries. The coexistence of other endemic diseases widely prevalent in developing countries, such as respiratory and gastrointestinal infections, complicate treatment and pose additional problems for medical personnel caring for HIV-infected individuals.

The Epidemic in the United States

The HIV/AIDS epidemic in the United States continues to expand.[3,5,6,7] In addition, use of antiretro viral therapy (ART) is now associated with a series of side effects and long term complications that may have a negative impact on mortality rates. HIV infection rates are continuing to climb among women, racial and ethnic minorities, young homosexual men, individuals with addictive disorders, and people over 50 years of age.[8] The appearance of multi-drug resistant strains of HIV presents an additional serious public health concern.[9,10,11] These data forebode an epidemic of even greater magnitude in the coming years. According to CDC reports, approximately one quarter of the HIV-infected population in the United States also is

[3] "The Future of AIDS," *Foreign Affairs,* November/December 2002.

[4] "Report on the Global HIV/AIDS Epidemic: July 2002," (UNAIDS/WHO, Geneva, Switzerland, 2002).

[5] "Cases of HIV Infection and AIDS in the United States, 2003", HIV/AIDS Surveillance Report, (CDC, 2004).

[6] "Centers for Disease Control and Prevention HIV Prevention Strategic Plan Through 2005," (CDC, 2001).

[7] "Cases of HIV Infection and AIDS in the United States, by Race/Ethnicity, 1998-2002", HIV/AIDS Surveillance Supplemental Report (CDC, 2004).

[8] Characteristics of Persons Living with AIDS and HIV, 2001", HIV/AIDS Surveillance Supplemental Report (CDC, 2003).

[9] N. Loder, *Nature* 407, 120 (2000).

[10] H. Salomon et al., *AIDS* 14, 17 (2000).

[11] "World Health Report on Infectious Diseases: Overcoming Antimicrobial Resistance," (WHO, Geneva, 2000).

infected with hepatitis C virus (HCV). HFVTHCV co-infection is found in 50 to 90 percent of injecting drug users (IDUs). HCV progresses more rapidly to liver damage in HIV-infected persons and may also impact the course and management of HIV infection, as HIV may change the natural history and treatment of HCV.[12]

AIDS disproportionately affects African Americans and Hispanics. "According to CDC figures for 2003, approximately 60 percent of newly infected women were African American and 20 percent were Hispanic. Among newly infected men, approximately 40 percent were African American and 22 percent were Hispanic.".[13]

The NTH AIDS Research Program

The NIH response to this epidemic requires a unique and complex multi-institute, multi-disciplinary, global research program. NIH has developed a comprehensive biomedical and behavioral research program to better understand the basic biology of HIV, develop effective therapies to treat and control HIV disease, and design interventions to prevent new infections from occurring. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of the NIH Institutes and Centers. This diverse research portfolio demands an unprecedented level of scientific coordination and management of research funds to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that research dollars are invested effectively and efficiently. It is the unique role of the Office of AIDS Research (OAR), part of the Office of the Director, to plan and coordinate all AIDS-related research across the NIH, thus allowing NIH to pursue a united research front against the global AIDS epidemic.

Program Assessment Rating Tool (PART): Assessment of NIH AIDS Program

The NIH AIDS program received an overall score of 83 in the OMB's FY 2005 Program Assessment Rating Tool (PART). This score included a 100 percent in the Program Purpose and Design section. The PART demonstrated that NIH provides effective scientific coordination and management of this diverse AIDS research portfolio through a comprehensive planning and budget development process, which was utilized to develop the FY 2006 budget request. NIH is enhancing collaboration, minimizing duplication, and ensuring that research dollars are invested in the highest priority areas of scientific opportunity that will allow NIH to meet its scientific goals.

Setting the AIDS Research Priorities: Comprehensive Plan and Budget

The Office of AIDS Research (OAR) develops an annual *NIH Plan for HIV-Related Research* that is based on the most compelling scientific priorities that will lead to better therapies and prevention strategies for HIV infection and AIDS. OAR has established an effective model for

[12] "Frequently Asked Questions and Answers About Confection with HIV and Hepatitis C Virus" (CDC, 2002).

[13] "Cases of HIV Infection and AIDS in the United States, 2003", HIV/AIDS Surveillance Report, (CDC, 2004).

developing a consensus on the scientific priorities of the Plan, utilizing planning groups composed of NIH scientists and experts from academia and industry, as well as representatives from the AIDS community, who meet to develop the Plan.

The Plan serves as the framework for developing the annual NIH AIDS budget; for determining the use of NIH AIDS-designated dollars; for tracking and monitoring expenditures; and for informing the scientific community, the public, and the AIDS-affected community about NIH AIDS research priorities, hi collaboration with the Director of NIH, the OAR determines the total annual NIH AIDS research budget. Within that total, the OAR establishes the AIDS research budgets for each NIH Institute and Center, in accordance with the priorities and objectives of the plan. This budget request is framed on the scientific priorities and objectives of the *NIH FY 2006 Plan for HIV-Related Research.* The entire plan can be found on the OAR web site: http://www.nih.gov/od/oar/public/pubs/fy2006/00 Overview FY20Q6.pdf

The FY 2006 research agenda continues the following over-arching themes: a strong foundation of basic science; research to prevent and reduce HIV transmission, including vaccines, microbicides, and behavioral interventions; research to develop better therapies for those who are already infected; international research, particularly to address the pandemic in developing countries; and biomedical and behavioral research targeting the disproportionate impact of AIDS on minority populations in the United States, hi particular, this budget request places highest priority on the discovery, development, and pre-clinical testing of additional HIV vaccine candidates. The evaluation of an AIDS vaccine will require extensive testing in the US and in international settings where there is a high incidence of HIV. High priority is placed on funding to move promising vaccine candidates into large-scale clinical trials to evaluate the potential for efficacy.

The Plan establishes the NIH AIDS research agenda in the following Scientific Areas of Emphasis: Natural History and Epidemiology, Etiology and Pathogenesis, Therapeutics, Vaccines, and Behavioral and Social Science. The Plan also addresses the cross-cutting areas of: Racial and Ethnic Minorities; Women and Girls; Microbicides; HIV Prevention Research; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination. The key priorities for each research area and directions for future research are summarized in this document.

VACCINES

RESEARCH PRIORITIES OF THE FY 2006 PLAN

- Maintain a vigorous program of basic and preclinical research for discovery, preclinical evaluation, and introduction of new vaccine candidates and immunization concepts.
  Support basic vaccine design research, particularly innovative research on immune responses to HIV envelope.
- Support basic research on the identification of correlates of immune protection: study the development and maintenance of effective immune responses to HIV antigens, particularly at mucosal surfaces, and address issues related to improvement in the duration of potentially protective immune responses.
  Implement direct "head-to-head" and comparative studies to assess immune responses in both preclinical and clinical evaluation of HIV vaccine candidates. Develop reagents, assays, and animal models to facilitate comparative vaccine studies. Identify, develop, and produce virus stocks for shared use in non-human primate models. Expand assessments of cellular immunity and neutralizing antibodies in central laboratories using validated assays and provide broader access to specimens for both academic and industrial investigators.
  Conduct appropriate preparative work in trial sites, particularly in international sites and minority communities, to provide critical viral and immunological information to inform vaccine trial design while helping to develop a strong, sustainable research infrastructure.
  Develop and implement a defined plan with specific goals to educate high-risk populations and communities in the United States and at international sites about HIV vaccines.

Safe and efficacious vaccines to prevent HIV infection and disease and/or transmission are essential for global control of the AIDS pandemic. As a result of increased funding from NIH in the area of HIV vaccines, many new approaches are being pursued. Basic research in vaccine design and studies of immune responses in small animals and non-human primates (NHP), as well as vaccine product development are underway. Recent HIV vaccine research studies in animal models have provided strong scientific rationales to further explore and develop several vaccine concepts and to move additional candidate vaccines into clinical testing. Although production of candidate vaccines for clinical study has proceeded slowly, at least 4-8 new candidate vaccines will enter Phase I trials in the next 2 years. Several new combinations of products, which are expected to provide better immune responses, also will be tested in Phase I or II trials. The Dale and Betty Bumpers Vaccine Research Center recently launched the first Phase I clinical trial of a multi-clade, multi-gene vaccine candidate.

VACCINE RESEARCH ACCOMPLISHMENTS

More than 35 products or combinations tested in over 68 Phase I and II trials with more than 4,200 volunteers
New vaccine designs developed; 4-8 to enter Phase I clinical trials within 2 years
First multi-gene, multi-clade Phase I trial launched by NIH Vaccine Research Center

NIH continues to increase support for a broad program encompassing basic, preclinical, and clinical research on candidate vaccine products. As promising candidates move further in the vaccine pipeline, expanded trials with populations at increased risk for HIV infection will become increasingly important. HIV/AIDS vaccine research requires trained health care, medical research, and prevention specialists, as well as populations at risk who will be integrally involved

in the development of vaccine candidates and clinical vaccine and prevention trials. International and domestic sites are being developed, including a cadre of trained personnel, to conduct vaccine trials.

One of the foremost priorities for testing candidate vaccines continues to be a resolution of the crisis in the supply of monkeys available for HIV/AIDS vaccine studies. The supply of non-human primates (NHP), particularly rhesus macaques, for AIDS research and other areas of biomedical research remains a major problem for NIH-funded investigators. Both the supply of animals and the available space for conducting experiments that require adequately controlled biosafety housing are limiting and impeding exploration of new concepts in HIV vaccines. NIH is working to find solutions to these obstacles.

The development of an HIV vaccine is a complex research challenge because HIV is unusually well-equipped to elude immune defenses, as exemplified by its ability to vary extensively, to persist in viral reservoirs, and to eventually overcome the immune system. Many different vaccine approaches are being pursued. Initial studies are leading to more advanced vaccine candidates that may provide better protection. NIH has now conducted approximately 70 Phase I and two Phase II clinical trials of nearly 40 vaccine candidates, individually or in combination, in human volunteers in collaboration with academic investigators and industry co-sponsorship.

THERAPEUTICS

RESEARCH PRIORITIES OF THE FY 2006 PLAN

- Advance the discovery and validation of new viral and cellular targets; Develop new therapeutic agents and regimens that: target drag-resistant virus; have activity in viral reservoirs and cellular compartments; and have improved pharmacologic and toxicologic properties, adherence potential and reduced cost.
  Determine optimal therapeutic strategies including when to start (early versus late), change, sequence, or interrupt therapies and evaluate therapeutic drag monitoring strategies.
  Target affected populations, especially women, injecting drag users (IDUs), children, adolescents, older adults, and across racial/ethnic groups. Conduct studies that permit evaluation of potential differences in response to therapy due to gender and/or racial/ethnic differences.
  Enhance capabilities for long-term followup and evaluate the long-term effects of therapy and the implications of these findings on public health.
  Develop safe, effective, feasible, and conveniently administered strategies to interrupt mother-to-child transmission (MTCT) of HIV with a focus on resource-limited settings and on breastfeeding.
  Conduct studies to evaluate and reduce short- and long-term toxicity of ARVs to prevent HIV transmission in women during pregnancy, and in their offspring who were perinatally exposed.
  Evaluate the effects of and develop treatments for co-infections, especially with hepatitis B virus (HBV), hepatitis C virus (HCV), tuberculosis (TB), or malaria, on the management of HIV disease.
  Design and conduct clinical studies that are appropriate for diverse international settings
  Evaluate the clinical and public health impact of ART and of prophylactic and therapeutic interventions for co-infections/opportunistic infections (OIs), AIDS-related malignancies, and other cancers.

Many HIV-infected people are living with the benefits resulting from NIH-supported therapeutics research. The development of combination regimens including protease inhibitors has extended the length and quality of life for many HIV-infected individuals in the United States and Western Europe. The use of antiretroviral therapy (ART) continues to result in the significant reduction of viral load, increased CD4 cell counts, decreased OIs and certain malignancies, and improved immune function in patients who are able to adhere to the treatment regimens and tolerate the toxicities associated with antiretroviral drugs. A high priority of NIH-sponsored AIDS therapeutics research continues to be the development of better drugs and therapeutic regimens that are less toxic and have fewer side effects, limit the development of drug resistance, enter viral reservoirs to inhibit viral replication, promote easier adherence, and are more readily accessible. Research is addressing the metabolic complications, including insulin resistance, and body composition changes such as deforming deposits of abdominal adipose tissue, that have emerged in individuals who have been on long-term antiretroviral regimens. More deaths occurring from liver failure, kidney disease, and cardiovascular complications are being observed in this patient population. The global impact and continued spread of the AIDS pandemic in both developed and developing nations underscore the urgent need to develop therapeutic regimens that can be implemented in international settings.

THERAPEUTICS RESEARCH ACCOMPLISHMENTS

Extended and improved quality of life for many HIV-infected individuals

Reduced AIDS deaths

Decreased morbidity due to opportunistic infections

Reduced pediatric mortality

Demonstration that combinations of antiretroviral agents can significantly reduce viral load in many patients to undetectable levels and increase CD4 counts

Revolution in design and testing of drugs and diagnostic methodologies benefits other diseases

Findings contributed to approval of AIDS-related therapies by FDA and development of guidelines for their optimal use

Antiretroviral and 01 prophylaxis regimens are becoming increasingly complex with respect to drug-drug interactions and adherence. Protease inhibitors, in particular, interact with each other and many other medications commonly used by HIV-infected individuals. A goal of research is minimizing viral replication and delaying disease progression, drug resistance, and development of clinical complications. Important studies are planned to evaluate delayed and long-term effects of these antiretroviral drugs.

The scientific agenda for NTH AIDS therapeutics research is focused on the following questions: Are there new viral and cellular targets against which therapies can be directed? What therapeutic agents and regimens can be developed that target drug-resistant virus? What are the optimal approaches for management of HIV infection, including when to start, change, sequence, or interrupt therapy? What are the effects of these drugs in pregnant and breastfeeding women, and what impact does this have upon the fetus? What is the impact of co-infection or cancer on disease progression and treatment of both HIV and comorbidities such as hepatitis B virus, hepatitis C virus, tuberculosis, or malaria? What are the clinical and public health ramifications of administering ART in developing countries? Collaboration between Government- and industry-sponsored drug development research and clinical trials is critical to achieve the common goal of developing therapeutic regimens that slow disease progression, extend life spans, and improve the quality of life for HIV-infected individuals.

RESEARCH PRIORITIES OF THE FY 2006 PLAN

- Facilitate the translation of new insights into HIV biology to develop novel interventions for the prevention and treatment of HIV infection. Identify and validate cofactors for viral genes as new targets capitalizing on novel technologies including viral interference and genomic screening.
- Elucidate the biologic determinants of HIV transmission between individuals, and define the mechanisms by which host factors, viral factors, and cofactors may influence the process of virus transmission and dissemination.
  Understand the dynamics of virus-host interaction through the course of HIV infection.
  Investigate the mechanisms of persistence of HIV infection.
  Develop innovative technologies in human and nonhuman primate immunology to guide vaccine development and immune reconstitution efforts.
- Advance the understanding of the mechanisms responsible for the toxicities and long-term complications of antiretroviral therapy (ART) and the factors that underlie changes in the causes of morbidity and mortality in an era of increasingly effective therapies.

Tremendous progress has been made in understanding the fundamental steps in the life-cycle of HIV, the host-virus relationship, and the clinical manifestations associated with HIV infection and AIDS. Groundbreaking research on basic HIV biology and AIDS pathogenesis has revolutionized the design of drugs, the methodologies for diagnosis, and the monitoring for efficacy of antiviral therapies. Maintaining a strong commitment to basic research is of paramount importantance in our fight against HIV/AIDS. This research is focused on gaining a better understanding in two areas: (1) how HIV infection is established and maintained, and (2) what causes the profound immune deficiency and severe clinical complications that accompany this infection.

ETIOLOGY AND PATHOGENESIS ADVANCES

Identification of key HIV components as drug targets
Identification of macromolecular structure of viral components for drug design
Identification of chemokines as co-receptors
Identification of viral reservoirs as sites of latent infection

Critical questions in this area are: What role do specific HIV proteins play in the viral life cycle in individual cells and within the bodies of infected individuals? What are the primary modes of HIV transmission between cells and between individuals? What contribution does the immune system make to controlling the infection and to the disease process? What mechanisms are involved in cell injury and death in the immune, nervous, and other organ systems affected by HIV? What host factors and cofactors influence primary infection and the course and outcome of HIV infection? What is the relationship of HIV infection to the associated malignancies, OIs and coinfections, neurological impairments, and metabolic disturbances that characterize AIDS? This basic knowledge is critical for our efforts to prevent and control HIV infection and disease progression.

Research is focusing on the different mechanisms of viral persistence to understand the reasons for drug failure, to design rational approaches for virus eradication, and to better assess the impact of persistence on HIV transmission and its implications for HIV prevention. HIV can persist in a latent reservoir of resting memory CD4 T cells that is established very early after

infection and by continuously replicating, albeit at very low levels, even in the presence of antiretroviral therapies that can drive viral load below the limits of detection.

Understanding the normal development and functioning of the human immune system is crucial to our ability to understand the effects of HIV on the immune system and the pathogenesis of AIDS. This understanding also holds the key to designing rational immune reconstitution approaches in persons undergoing antiretroviral treatment and identifying the characteristics of the immune response that are needed for a protective vaccine.

The basic science underlying HIV etiology and pathogenesis research is generally gender neutral. Basic mechanisms of viral replication and pathogenesis are not expected to differ in women and men. However, there are differences in the way HIV infection is transmitted and how the disease is manifested in women and men. Studies have been designed to elucidate the pathogenic mechanisms more commonly observed in women, children, and adolescents infected with HIV. Transmission of HIV from a mother to her infant may occur *in utero* through transplacental passage of virus, during delivery, or after birth through breast-feeding. Many basic research questions associated with maternal-fetal transmission remain unclear and are actively under investigation.

AIDS is associated with a broad spectrum of cancers and tumors. As HIV causes immunosuppression and most AIDS-associated malignancies are strongly associated with viruses, HIV infection provides a unique model to study the interplay of viruses, a dysfunctional immune system, and the development of cancers. Elucidation of the interactive factors involved in the pathogenesis of AIDS-associated malignancies will possibly translate into the identification of new targets for prevention and treatment.

HIV infection results in the progressive damage of the immune systems of infected individuals and makes them susceptible to a diverse collection of bacteria, viruses, fungi, and protozoa that represent the major causes of suffering and death for HIV-infected individuals. Opportunistic infections remain one of the most important complications of HIV infection and the principal cause of death in AIDS patients. Understanding the fundamental biology and pathogenesis of these organisms, their interaction with the host immune system, and the effect of therapy-associated immune reconstitution on the clinical course and manifestations of OIs will translate into new or more rational approaches to the prevention and treatment of OIs in patients on ART, as well as in patients who lack access to or who are not responding to ART. HIV infection is also associated with multiple endocrine alterations, probably reflecting critical interaction between the endocrine and the immune systems. HIV-associated hematologic, pulmonary, cardiac and vascular, renal, mucocutaneous, bone, and liver complications also represent causes of morbidity in infected subjects. Some of these complications are disproportionally affecting racial groups. The pathogenic mechanisms involved in all these AIDS manifestations are not well understood and are under investigation. Their definition will permit a more rational approach to both preventive and therapeutic interventions.

RESEARCH PRIORITIES OF THE FY 2006 PLAN

Sponsor domestic and international epidemiologic studies to characterize modes of transmission, including host characteristics (e.g., sexual behavior, substance use, use of blood products and other injections, effects of treatment, genetic variations) and viral characteristics, or continued risk behaviors in HIV-infected and uninfected populations of adults, adolescents, and children.

Develop, maintain, and effectively utilize domestic and international cohorts, repositories, and nested studies among populations experiencing emerging and ongoing HIV epidemics to establish databases that support analyses of host and viral characteristics. Use this approach to: assess the impact of interventions on HIV-related outcomes through operations research; and evaluate treatment effectiveness at the individual and population levels.

Implement epidemiologic and simulation studies to inform, monitor, and evaluate intervention strategies and to optimize surveillance in domestic and international settings.

Develop and evaluate accurate, reproducible, and affordable virologic, immunologic, pharmacologic, and genetic assays; measures of adherence to therapy; markers of toxicity and comorbidity, and markers of recent infection for use in domestic and international settings; and HIV-related normative parameters for clinical and laboratory settings in resource-limited countries.

Natural history and epidemiologic research is needed to monitor epidemic trends, develop and evaluate prevention modalities, follow the changing clinical manifestations of HIV disease in different populations, and measure the effects of treatment regimens. NIH will continue to support research to examine topics in HIV transmission, HIV/AIDS disease progression (including the occurrence of opportunistic infections), malignancies, metabolic complications, neurological and behavioral dysfunctions, and the development of other HIV/AIDS-related conditions. Domestically, as well as internationally, the populations affected by HIV/AIDS are also those most severely affected by the spreading epidemics of sexually transmitted diseases (STDs), TB, and other co-morbidities, such as Hepatitis C. Researchers are studying the effects of viral, host, and other factors on transmission and disease progression. Since biological, pharmacological, physiological, and behavioral factors all potentially influence the impact of antiretroviral therapies on HIV transmission, researchers are evaluating the specific contributions of these factors and their net impact on HIV transmission. Research also is focusing on determining the biological characteristics, sociocultural factors, and health services issues that contribute to the differential dynamics of HIV transmission and disease progression in men, women, and in different racial/ethnic groups. Results from these studies will provide new directions and improvements in HIV/AIDS prevention and care. NIH will continue to emphasize the importance of epidemiologic studies to investigate the mechanisms of disease progression, the causes of death, and the impact of therapy in changing the spectrum of HIV disease. The expansion of existing study populations in the United States will allow the identification of long-term effects of HIV therapy. The assembly of new, representative cohorts, specimen repositories,

NATURAL HISTORY AND EPIDEMIOLOGY RESEARCH ACCOMPLISHMENTS

- CD4 and viral load established as biomarkers for disease progression and response to therapy
- Gender differences: women seroconvert at lower viral load than men
- Regimens to prevent opportunistic infections initiated at 200 CD4 level or less
- Presence of Hepatitis G virus (GBV-C) predicts survival

and databases in developing countries will be important to study key co-factors that modify HIV disease. NIH will foster basic and applied research to develop inexpensive virologic, immunologic, and genetic assays for use in domestic and developing country settings.

MICROBICIDES

RESEARCH PRIORITIES OF THE **FY 2006 PLAN**

- Foster the development of microbicides consisting of exogenous and endogenous agents and based on specific biological and physiological pathways involving HIV transmission across the epithelia.
  Identify and standardize relevant, practical, and accessible methodologies to assess preclinical/clinical safety and activity of microbicides.
  Foster the development of combination approaches, such as chemical and physical barriers, and of microbicides containing multiple active compounds with different chemical classes, specificities, and mechanisms of action in acceptable formulations to prevent transmission and acquisition of HIV and other sexually transmitted infections.
  Promote innovative methods to develop and assess acceptable formulations and modes of delivery for microbicides.
  Expand capacity (infrastructure and human resources) and strengthen coordination to conduct Phase II/III microbicides clinical trials.
  Conduct social and behavioral research in concert with microbicides clinical trials, including research on product use, user acceptability, sexual behaviors, and the identification and development of reliable and valid behavioral tools and measurement techniques for use in trials.
  Promote innovative mechanisms of funding to attract additional investigators to undertake multidisciplinary research on microbicides discovery and development.

The vulnerability of women to acquiring HIV infection requires the development of effective and acceptable female-controlled chemical and physical barrier methods, such as topical microbicides, to reduce HIV transmission. NIH supports a comprehensive research program that includes the screening, discovery, development, preclinical *in vitro* and *in vivo* testing, and clinical evaluation of compounds with the potential to act as antimicrobial agents with both spermicidal and nonspermicidal activity. NIH closely collaborates with academia and industry to identify and explore new and existing compounds as potential topical microbicidal agents.

The Office of AIDS Research coordinates microbicide research across the NIH, and with other federal agencies providing administrative accountability and funding coordination for this important research area.

Animal model testing and toxicity studies of potential candidate compounds are conducted through NTH-sponsored contracts before these agents are considered for clinical trials. NIH also supports Phase I, II, and III clinical trials of various topical microbicides, as well as behavioral and social research on the acceptability and use of microbicides among different populations. Important areas of research include the establishment of clinical trial sites and the necessary infrastructure to conduct those trials, especially in developing countries; the development of criteria for selecting potential products to be evaluated in clinical trials and for advancing them through the different phases of clinical studies; and research on ethical and behavioral issues impacting clinical trials.

RESEARCH PRIORITIES OF THE FY 2006 PLAN

Develop and test comprehensive behavioral models for risk of HIV transmission and acquisition.
Elucidate new and changing patterns, contexts, and kinds of drug and alcohol use and their implications for HIV transmission and acquisition, either directly or as mediators of sexual behavior.
Develop and evaluate methods of intervening to reduce HIV acquisition and transmission associated with drug and alcohol use.
Develop and evaluate methods of intervening to reduce HIV acquisition and transmission associated with sexual behavior, using methods that recognize the implications of technological advances in medicine (e.g., rapid HIV testing, medications to treat sexual dysfunction) and changes in medical practice (e.g., simplified dosing regimens, routine and universal testing).

- Support research on the interactions among factors that contribute to the concurrence of HIV/AIDS and other medical disorders (e.g., infectious diseases, substance abuse) and social problems, and develop interventions to address the co-occurring conditions.
- Improve understanding of health disparities in consequences and of care for HIV infection in various subpopulations and of the stigma associated with HIV/AIDS.

NIH supports research to further our understanding of how to change the behaviors that lead to HIV transmission—including preventing their initiation—and how to maintain protective behaviors once they are adopted in all populations at risk. NIH sponsors research related to: developing, implementing, and evaluating behavioral and social interventions to reduce HIV transmission in a range of populations and settings; strengthening our understanding of the determinants, trends, and processes of HIV-related risk behaviors and the consequences of HIV infection; developing and evaluating behavioral strategies for preventing or ameliorating the negative physical, psychological, and social consequences of HIV infection; and improving the methodologies employed in behavioral and social science research. A better understanding of social and cultural factors associated with HIV risk or protection, particularly in minority communities, will contribute to the successful implementation of a broader range of preventive or therapeutic measures. Drug users and their sex partners are the fastest growing segment of AIDS cases in the U.S. and in many other countries. Priority is being given to research that bridges and builds upon studies of the phenomenon of addiction itself, the complex interaction of alcohol use, drug use, and poor impulse control, and to developing effective HIV-related interventions from that knowledge base.

The development of new and more effective anti-HIV drugs and drug combinations has raised a host of behavioral issues. Lack of complete adherence to drug regimens may result in the development of drug-resistant strains of HIV, which could have devastating public health implications. In addition, HIV-infected individuals taking antiretroviral therapies who experience improved health and a decline in detectable virus may believe that they are less infectious and may lapse into unsafe sexual and drug-using behaviors. This could have the effect of increasing HIV transmission, if the virus is still viable at undetectable levels. These issues highlight the importance of research on how best to ensure adherence to both pharmacological and behavioral HIV-related interventions.

RESEARCH PRIORITIES OF THE FY 2006 PLAN

Examine the ways in which social, economic, cultural, and environmental conditions, including stigma and discrimination, contribute to, or create sources of, HIV-related risk; and develop interventions based on this understanding.

Examine factors associated with the initiation and sustainability of HIV prevention efforts among individuals and communities over time, as well as factors that may impede consistent HIV risk reduction practices.

Elucidate the effects of HIV/AIDS treatment availability, delivery, success, and failure on HIV transmission and acquisition, and the integration of prevention into clinical care.

Further explore, develop, and evaluate alternative methods to the randomized controlled trial (RCT) for testing the efficacy of multidisciplinary HIV preventive interventions when RCTs are inappropriate or impossible to conduct; and develop guidelines to inform the field about when such non-RCT methods are appropriate to employ.

In collaboration with other governmental and nongovernmental organizations, enhance support for operations, health services, and evaluation research on the design, adaptation, testing, and implementation of evidence-based HIV prevention strategies; and assess the impact of such strategies on risk behaviors at the population level.

NIH supports a comprehensive prevention science research agenda that targets interventions to both infected and uninfected at-risk individuals to reduce HIV transmission. Biomedical prevention research priorities include the development of topical microbicides, strategies to prevent mother-to-child transmission (including a better understanding of HIV risk associated with breast-feeding), and management of sexually transmitted diseases (STDs). NIH behavioral research strategies include interventions related to drug and alcohol use and risky sexual behaviors. Research efforts continue to identify the most appropriate intervention strategies for different populations and sub-epidemics in the United States and around the world.

PREVENTION RESEARCH AGENDA

- Vaccines
- Topical microbicides
- Behavioral research
- Reducing transmission due to substance abuse
- STD control
- Prevention of mother-to-child transmission
- Antiretroviral therapy as prevention

These HIV prevention research activities include both basic and intervention studies. Research that elucidates the fundamental mechanisms of human behavior and disease transmission and progression provides the essential basic knowledge needed for the development of testable interventions. Studies examine the range and interaction of biological, neurological, psychological, familial, social network, and other environmental factors that have an impact on HIV transmission, acquisition, or protection. While the focus of the NIH HIV prevention research program is on primary prevention of new HIV infections, it also addresses secondary prevention, that is, prevention of the negative physiological, psychological, and social consequences of disease among individuals already infected with HIV and their families, networks, and communities. This includes identifying potential co-factors, correlates, and mediators of disease progression, and developing biomedical and/or psychosocial interventions to address them.

RESEARCH PRIORITIES OF THE FY 2006 PLAN

- Enhance the capacity of minority investigators, minority institutions, and minority community-based organizations to conduct multidisciplinary HIV research
- Identify biomedical, sociocultural, and structural determinants, pathways, and mechanisms that maintain or perpetuate health disparities.
- Develop and test innovative models, research methods, and measures of risk behavior in racial and ethnic minority areas.
- Further explore the natural history of HIV disease and its consequences for racial and ethnic minority communities.
- Include racial and ethnic minorities in clinical research in numbers that reflect their representation in the HIV epidemic.

HIV infection, like many other disease states, reflects the ongoing health disparities among racial and ethnic minority communities. Prevalence of HIV infection in racial and ethnic minority communities is disproportionately higher than in majority communities. In many U.S. urban centers, the prevalence of HIV infection mimics rates found in the developing world. These findings, along with the resurgence of STDs and associated high-risk behaviors, underscore the need for comprehensive strategies to decrease HIV transmission in affected vulnerable populations, and improve treatment options and treatment outcomes.

MINORITY INITIATIVES

- Minority-targeted research, primarily prevention
- Initiatives to increase minority enrollment in clinical studies
- Minority training, infrastructure, and research capacity-building initiatives
- Grantsmanship workshops for minority researchers
- Regional Technology Transfer Program
- Community outreach programs

NIH is directing increased resources toward research to develop new interventions that will have the greatest impact on these groups. These include interventions that address the co-occurrence of other STDs, hepatitis, drug abuse, and mental illness; and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities. NIH is making significant investments to improve research infrastructure and training opportunities for minorities and will continue to assure the participation of minorities in ADDS clinical trials, as well as in natural history, epidemiologic, and prevention studies. NTH has provided additional funds to projects aimed at increasing the number of minority investigators conducting behavioral and clinical research; targeting the links between substance abuse, sexual behaviors, and HIV infection; increasing outreach education programs targeting minority physicians and at-risk populations; and expanding the portfolio of population-based research. One of these projects is a series of Training and Career Development Workshops for racial and ethnic minority investigators. These workshops provide minority investigators with an opportunity to learn more about available NIH funding mechanisms and to meet and network with senior minority investigators who receive significant levels of NIH funding.

NIH supports a broad array of behavioral intervention studies with specific focus on African American populations. These studies are characterizing the disease process in drug users, factors influencing disease progression, consequences of multiple co-infections, effectiveness of therapeutic regimens, and the impact of health care access and adherence to therapeutic regimens on disease outcomes. The increasing number of AIDS cases among minorities underscores the importance of research to define and utilize cultural, social, and contextual factors that affect HIV risk behaviors. The role of alcohol and drug use in facilitating HIV transmission through social networks in all communities also is being explored within these social frameworks.

WOMEN AND GIRLS

RESEARCH PRIORITIES OF THE FY 2006 PLAN

Study the biology of the reproductive tract of HIV-infected and HIV-uninfected women and girls, integrating studies of physiology, immunology, microbiology, and anatomy.

- Elucidate a range of host-virus interactions through the course of HIV infection (in particular, during primary HIV infection) and across the life cycle in women and girls.
- Develop and continue clinical studies—including biological, therapeutic, vaccine, natural history, epidemiological, behavioral, and social science—to ascertain the effects of sex and gender in HIV infection among women and girls.

Enhance basic behavioral and social science research (theoretical and methodological) on gender construction, maintenance, dynamics, and consequences—including gender-based stigma and discrimination; and integrate this work into the design and evaluation of HIV prevention and care interventions.

- Explore factors that influence development, adoption, use, and effectiveness of women-controlled methods (including physical and chemical barrier methods), alone or in combination, for preventing HIV transmission and acquisition; and ensure dissemination of resulting information.

Enhance opportunities and mechanisms for recruiting and training biomedical, behavioral, and social scientists in the conduct of interdisciplinary sex and gender analyses in HIV/AIDS research.

Women experience HIV/AIDS differently from men both physiologically and socially. NIH research has demonstrated that women progress to AIDS at lower viral load levels and higher CD4 counts than do men. This finding may have implications for care and treatment of HIV-infected women, particularly with antiretroviral therapy. Women's childbearing capacity also differentiates their HIV/AIDS experiences from men's, as HIV-infected pregnant women may transmit the virus to their fetuses and infants. Women in most societies are the primary care providers for children and older people, so their early deaths from AIDS and its complications often leave dependents with no one to care for them. NIH researchers are studying the ways in which sex and gender confer vulnerability to, or protection from, HIV infection and ADDS among women and girls—in general, and relative to men—in diverse geographical settings and during different stages of the life course. There are many research questions that remain unanswered about specific anatomical and physiological characteristics of women and girls that might play a role in transmission, acquisition, or resistance to HIV infection. Studies will focus on factors in HIV acquisition, including the influence of hormonal modulation on viral replication and immune responses in the reproductive tract, and co-factors, such as coincident infections with other STD pathogens.

RESEARCH PRIORITIES OF THE FY 2006 PLAN

Develop in-country research and training infrastructure for the conduct of integrated prevention and treatment or care intervention research, integrating new activities into existing health care and prevention services where possible.

Define the spectrum of HIV-related disease and its response to treatment as it applies to diverse geographic settings, and develop integrated prevention and treatment interventions to limit the impact of HIV-related disease.

- Conduct studies (experimental and observational) to identify the appropriate modalities of introduction and long-term use of ART in resource-limited settings.

Support studies to identify effective, appropriate, and sustainable interventions to curtail HIV transmission. Such interventions should encompass the prevention of all transmission modalities and their mutual interaction.

Study and address barriers to the conduct of international research, including access to health and research facilities for at-risk populations, research regulatory requirements, consistent application of bioethics principles, and institutional factors.

Since the early days of the epidemic, NIH has supported research efforts in countries affected by HIV and AIDS. Beginning in 1984 with a research project in Haiti and the establishment Of Projet SIDA in 1985 in what was then Zaire, NTH has maintained a strong international AIDS research portfolio. NIH has expanded its research effort to encompass approximately 90 countries around the world. Results of this research benefit not only the people in countries where the research is conducted, but people affected by HIV/AIDS worldwide. NIH- sponsored international research includes efforts to develop: HIV vaccine candidates and chemical and physical barrier methods, such as microbicides, to prevent sexual transmission; behavioral strategies targeted to the individual, family, and community to alter risk behaviors associated with sexual activity and drag and alcohol use; drag and non-drag strategies to prevent mother-to-child transmission (MTCT); therapeutics for HIV-related co-infections and other conditions; and approaches to using ART in resource-poor settings.

NEW CHALLENGE: CLINICAL EVALUATION OF THERAPIES IN INTERNATIONAL SETTINGS

Expand therapeutic studies into international sites

~" Develop research capacity and infrastructure

Design studies to improve and facilitate delivery of therapeutic interventions

Evaluate clinical and public health impact of antiretroviral treatment

Integrate therapeutic regimens and prevention **interventions**

Before prevention and treatment interventions can be implemented in different geographic settings, their safety must be confirmed and efficacy demonstrated in such settings through clinical trials and other intervention research. To develop vaccines and other prevention strategies that will be effective globally, Phase I safety studies are first conducted in small populations in the U.S. To establish efficacy, large numbers of at-risk study participants are necessary. Around the world, the predominant mode of HIV transmission is heterosexual. Among heterosexuals in the United States, the rate of HIV infection is estimated to be

approximately 1.5 percent. In some developing counties, the rate of heterosexual HIV infection is 13-25 percent. Because of the large populations at high risk of infection, prevention studies can be more efficiently conducted in those settings.

Although industrialized nations have experienced a dramatic decrease in transmission of HIV from infected mother to her child, preventing this transmission is a significant challenge in resource-poor settings of the world; strategies that can effectively be used in such settings continue to be pursued.

Development of a research infrastructure is essential to these research programs. Specific international infrastructure needs include: (1) developing research sites through establishment of stable, targeted cohorts, development of recruitment strategies, and enhancement of laboratory, clinical, and data management capabilities; (2) increasing the number of scientists, clinicians, and health care workers trained in basic, clinical, and behavioral research, data management, and ethical considerations; (3) developing research collaborations; and (4) transferring appropriate clinical and laboratory technologies.

TRAINING, INFRASTRUCTURE, AND INFORMATION DISSEMINATION

RESEARCH PRIORITIES OF THE **FY 2006** PLAN

Continue to support training of domestic and international biomedical and behavioral AIDS researchers.

Continue to support improvement of facilities and equipment for the conduct of domestic and international AIDS research, including support of facilities for animal model research.

Continue to support effective information dissemination approaches among researchers, health care providers, and affected communities to rapidly translate research findings into practice.

NIH will continue to support training of domestic and international biomedical and behavioral AIDS researchers, as well as the improvement of facilities and equipment for the conduct of AIDS-related research, including facilities for animal model research. Numerous NIH-funded programs have increased the number of training positions for AIDS-related research, including programs specifically designed to recruit individuals from minority communities into research careers and to build research infrastructure in minority institutions. The NIH Loan Repayment Program (LRP) was mandated by Congress under Public Law 100-607 in 1988 and authorized under 42 USC 288-1 to encourage health professionals to engage in AIDS-related research at NIH. NIH also sponsors programs to train scientists in developing countries to undertake AIDS research. The National Primate Research Centers (NPRC) Program, provides specialized facilities, scientific and technical personnel, animal models research and breeding, and a wide variety of non-human primate species to support diverse requirements for AIDS-related research.

Effective information dissemination approaches will continue to be integral to HIV prevention and treatment efforts. Such programs are critical in light of the continuing advent of new and complex antiretroviral treatment regimens, the adherence issues related to HIV/AIDS treatment, the need for research communities to work and communicate globally, and the need to translate

behavioral and social prevention approaches into practice. The changing pandemic and the increasing number of HIV infections in specific population groups, such as minorities and women, also underscore the need to disseminate HIV research findings and other related information to communities at risk. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to rapidly translate research results into practice and to shape future research directions.

MANY **OTHER** DISEASE RESEARCH EFFORTS BENEFIT FROM **AIDS** RESEARCH

AIDS research is unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases. AIDS research has provided an entirely new paradigm for drug design, development, and clinical trials to treat viral infections. For example, the drug known as 3TC, developed to treat HIV/AIDS, is now the most effective therapy for chronic hepatitis B infection. Drugs developed to prevent and treat AIDS-associated opportunistic infections also provide benefit to patients undergoing cancer chemotherapy or receiving anti-transplant rejection therapy. AIDS research also is providing a new understanding of the relationship between viruses and cancer.

AIDS RESEARCH BENEFITS OTHER DISEASE RESEARCH

- New paradigm for viral research and drug design
- Established concept of "prophylaxis" of opportunistic infections in immuno-suppressed persons
- Provides unique model to study the role of the immune system in the emergence of cancers, and to test novel approaches by which immune responses can be modified to help treat malignancies (KS, NHL, cervical cancer)
- New approaches for rapid and sensitive diagnosis of disease and monitoring of treatment is applicable to other infectious diseases
- Understanding of HIV-associated wasting benefits persons with cancer and other diseases
- 3TC and other drugs and drug combinations developed for HIV now standard of care for Hepatitis B and C
- Drugs for opportunistic infections used for transplant or immuno-suppressed patients
- Design of clinical trials, including community involvement
- Understanding of immune response to pathogens
- Insight into neurological, autoimmune, and metabolic diseases

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research
SUMMARY BY BUDGET MECHANISM

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects						
Noncompeting	2,238	$1,205,183,000	2,146	$1,259,993,000	2,025	$1,018,459,000
Administrative supplements	(117)	62,565,000	(92)	17,930,000	(79)	16,176,000
Full Funded	0	0	0	0	0	0
Single Year	700	272,105,000	716	294,948,000	700	540,413,000
Subtotal, competing	700	272,105,000	716	294,948,000	700	540,413,000
Subtotal, RPGs	2,938	1,539,853,000	2,862	1,572,871,000	2,725	1,575,048,000
SBIR/STTR	61	26,988,000	66	27,885,000	64	25,389,000
Subtotal, RPGs	2,999	1,566,841,000	2,928	1,600,756,000	2,789	1,600,437,000
Research Centers						
Specialized/comprehensive	52	104,684,000	55	113,036,000	55	113,708,000
Clinical research	0	43,882,000	0	44,721,000	0	44,721,000
Biotechnology	1	6,272,000	1	6,406,000	2	6,789,000
Comparative medicine	20	49,537,000	27	50,256,000	27	54,314,000
Research Centers in Minority Institutions	0	8,373,000	0	8,470,000	0	8,470,000
Subtotal, Centers	73	212,748,000	83	222,889,000	84	228,002,000
Other Research						
Research careers	317	41,248,000	325	42,769,000	328	43,002,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	17	37,255,000	23	37,365,000	24	37,078,000
Biomedical research support	3	1,449,000	1	1,510,000	1	1,515,000
Minority biomedical research support	3	1,151,000	2	841,000	2	845,000
Other	104	55,165,000	118	60,309,000	117	62,940,000
Subtotal, Other Research	444	136,268,000	469	142,794,000	472	145,380,000
Total Research Grants	3,516	1,915,857,000	3,480	1,966,439,000	3,345	1,973,819,000
Ruth L. Kirschstein Trainins Awards:	FTTPs		FTTPs		FTTPs	
Individual awards	90	3,697,000	94	3,861,000	92	3,901,000
Institutional awards	735	33,320,000	741	34,140,000	703	33,688,000
Total, Training	825	37,017,000	835	38,001,000	795	37,589,000
Research & development contracts	191	396,476,000	211	415,886,000	184	429,769,000
(SBIR/STTR)	(6)	(1,470,000)	(5)	(1,187,000)	(5)	(1,187,000)
Intramural research		329,244,000		330,478,000		326,005,000
Research management and support		95,185,000		97,432,000		97,460,000
Construction		8,325,000		3,966,000		0
Library of Medicine		7,416,000		7,450,000		7,451,000
Office of the Director		60,432,000		60,899,000		60,899,000
Total, NIH Budget Authority		2,849,952,000		2,920,551,000		2,932,992,000
RoadMap Support		10,572,000		11,251,000		15,327,000

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Funding by the NIH Plan for HIV-Related Research
(dollars in thousands)

Research Area	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate	Change
Natural History and Epidemiology	$320,803	$321,115	$312,694	($8,421)
Etiology and Pathogenesis	735,314	737,369	703,204	(34,165)
Therapeutics	730,987	741,827	712,309	(29,518)
Vaccines	452,277	507,183	607,285	100,102
Behavioral and Social Science	415,398	417,766	411,856	(5,910)
Training and Infrastructure	155,270	155,207	148,125	(7,082)
Information Dissemination	39,903	40,084	37,519	(2,565)
Total, Budget Authority	2,849,952	2,920,551	2,932,992	12,441

National Institutes of Health

Office of AIDS Research

AIDS Funding by Institute and Center

Institute/Center	FY 2004 Actual	*tY* 2005 Appropriation	FY 2006 Estimate
NCI	$267,857,000	$265,907,000	$256,228,000
NHLBI	75,074,000	74,690,000	68,031,000
NIDCR	25,192,000	24,985,000	19,887,000
NIDDK	30,828,000	31,151,000	31,210,000
NINDS	47,155,000	47,364,000	46,819,000
MAID	1,396,836,000	1,459,642,000	1,504,469,000
NIGMS	54,570,000	54,632,000	54,025,000
NICHD	130,311,000	132,992,000	134,904,000
NEI	12,663,000	12,562,000	10,692,000
NIEHS	8,717,000	8,702,000	7,589,000
NIA	5,489,000	5,459,000	5,443,000
NIAMS	6,719,000	6,697,000	4,915,000
NIDCD	1,748,000	1,734,000	1,426,000
NIMH	181,219,000	182,615,000	180,362,000
NIDA	312,979,000	313,137,000	303,104,000
NIAAA	26,784,000	27,166,000	27,214,000
NINR	12,083,000	12,236,000	12,236,000
NHGRI	6,877,000	6,862,000	6,904,000
NIBIB	1,056,000	1,048,000	1,048,000
NCRR	152,544,000	156,858,000	162,618,000
NCCAM	2,800,000	2,778,000	2,308,000
NCMHD	—	—	—
FIC	22,603,000	22,985,000	23,210,000
NLM	7,416,000	7,450,000	7,451,000
OD	60,432,000	60,899,000	60,899,000
B&F	—	—	—
TOTAL, Budget Authority	2,849,952,000	2,920,551,000	2,932,992,000

NATIONAL INSTITUTES OF HEALTH
Office of the Director
Office of AIDS Research

SIGNIFICANT ITEMS IN HOUSE, SENATE, AND CONFERENCE APPROPRIATIONS COMMITTEE REPORTS

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108- 636)

Item

Microbicides - Microbicides, a class of products that would be applied topically to prevent HIV, represent a promising prevention strategy, with the potential to be especially significant in preventing HIV in women, who now account for more than half of the individuals newly infected with HIV globally. Once developed, microbicides and vaccines would serve as complementary HIV prevention technologies. The Committee is concerned that microbicide research at NIH is currently conducted with no single line of administrative accountability or specific funding coordination. The Committee urges NIH to consider establishing a lead office to coordinate research among institutes and with other Federal agencies.

Action taken or to be taken

The Office of AIDS Research (OAR), located in the Office of the Director, NIH, was established as the lead office to coordinate microbicide research among the NTH institutes and with other Federal agencies, providing a single line of administrative accountability and specific funding coordination. OAR plans, coordinates, and develops a trans-NIH plan and budget for all NIH AIDS research, including microbicide research. OAR has carried out its mandate and worked to accelerate this important field of research. In 2001, OAR developed the first *NIH Strategic Plan for Microbicides,* in parallel with the annual *NIH Plan for HIV-Related Research,* which establishes the scientific agenda for the conduct of NIH ATDS-related research. The Plan has been updated every year to reflect the most recent scientific advances and priorities in microbicide research. NIH staff and non¬ government experts, including other DHHS agencies (CDC, FDA) and other U.S. government agencies (USAJD) work together to develop the plan.

OAR provides funding oversight by developing an annual trans-NIH budget and allocating all appropriated AIDS research funds to the Institutes, based explicitly on the priorities and objectives of the strategic plan. The ICs submit their ADDS-related research budget requests to OAR based on the plan's priorities and objectives. OAR allocates the AIDS research budget levels to each IC. The allocation is based on the scientific priority of the proposed initiatives in relation to the Plan and to other IC submissions to eliminate redundancy and/or to assure cross-Institute collaboration. OAR consults regularly with the IC Directors and maintains knowledge of the ongoing microbicide portfolios supported by each IC. This funding coordination process ensures that NIH AJDS-related research funds will be provided to the most compelling scientific opportunities.

OAR established the Trans-NIH Microbicide Research Working Group, comprised of representatives from NIAJD, NIDA, NICHD, NIMH, FIC, and ORWH, to facilitate information sharing about ongoing and planned initiatives; facilitate collaborative research; and develop the annual strategic plan for microbides. OAR also developed the first *U.S. Government Strategic Plan for Microbicides* in coordination with CDC, FDA, and USAID. This Plan identifies the scientific agenda in microbicide research and summarizes each agency's current activities.

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108- 636)

Item

Office of AIDS Research- The O A R develops a comprehensive plan for N I H AIDS-related research activities which is updated annually. The plan is the basis for the President's budget distribution of AIDS-related funds to the ICs within N I H. The Committee expects the Director of N I H to use this plan and the budget developed by O A R to guide his decisions on the allocation of A I D S funding among the Institutes. The Director of N I H also should use the full authority of his office to ensure that the Institutes and Centers spend their ADDS research dollars in a manner consistent with the plan. In addition, the O A R allocates an emergency A I D S discretionary fund to support research that was not anticipated when budget allocations were made. (Page 106)

Action taken or to be taken

O A R completed the *NIH FY 2006 Plan for HIV-Related Research,* on which the FY 2006 President's budget request is based, and has initiated the FY 2007 planning process. The Plan initiates the annual budget development and allocation process. The budget is explicitly tied to the priorities and objectives that establish the scientific opportunities of the strategic plan. Based on those priorities and objectives, the ICs submit their AIDS-related research budget requests to O A R, focusing on new or expanded program initiatives for each scientific area. O A R reviews the IC initiatives in relation to the Plan, to O A R priorities, and to other IC submissions to eliminate redundancy and/or to assure cross-Institute collaboration. The N I H Director and the O A R Director together determine the total amount allocated for A I D S research within the overall N I H budget, as required by law. Within that total, O A R allocates the AIDS research budget levels to each IC, based on the scientific priority of the proposed initiatives, at each step of the budget development process up to the time of the final congressional appropriation. This involves consulting regularly with the IC Directors and maintaining knowledge of the ongoing scientific research programs and planned initiatives supported by each IC. This process allows O A R to ensure that N I H AIDS-related research funds will be provided to the most compelling scientific opportunities, rather than distributed simply by a formula. The careful determination of the balance of the research agenda between institutes, among areas of science, between AIDS and non-AIDS, between intramural and extramural, between basic and clinical, between investigator-initiated and targeted, requires a finely tuned knowledge of the science and of the institutes' portfolios.

The O A R maintains the AIDS Research Information System (ARIS) to track and monitor the use of AIDS funds. Each project funded with AIDS-designated dollars is reported to the A R I S and coded according to the objectives of the plan. As research progresses and knowledge expands, new scientific opportunities arise. O A R periodically reviews the N T H AIDS research portfolio to ensure that projects funded with AIDS-designated dollars are supporting the highest priorities of the A I D S research agenda.

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108- 636)

Item

Office of AIDS Research - The Committee has included the same general provisions in bill language that were contained in the 2004 appropriations bill. This language permits the Director of O A R, jointly with the Director of N I H, to transfer between Institutes and Centers up to three percent

of the funding determined by NIH to be related to AIDS research. This authority could be exercised throughout the fiscal year subject to normal reprogramming procedures, and is intended to give NIH flexibility to adjust the AIDS allocations among Institutes if research opportunities and needs should change. The Committee also repeats language from last year's bill making the research funds identified by NIH as being AIDS related available to the OAR account for transfer to the Institutes. This provision permits the flow of funds through the OAR in the spirit of the authorization legislation without requiring the Congress to earmark a specific dollar amount for AIDS research. (Page 106)

Action taken or to be taken

The Director of OAR in consultation with the Director of NIH will allocate all monies for AIDS-related research to the Institutes and Centers in accordance with the scientific priorities and objectives of the NIH FY 2006 Plan for HIV-Related Research. The Plan serves as the framework for developing the NIH AIDS budget as well as for determining the use of NIH AIDS-designated dollars. In addition, all AIDS-designated expenditures are coded and tracked in accordance with the objectives of the plan.

The OAR appreciates the critical flexibility that the 3 percent transfer authority provides to move funds to meet the scientific priorities. We will reserve the use of this critical authority for only the most pressing need that could not be addressed by use of other funding mechanisms, for example, if a scientific breakthrough required expanded clinical trials.

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108- 636)

Item

Office of AIDS Research - The Committee encourages OAR to strengthen science-based HIV prevention research for African Americans, Latinos, Native Americans, Asian Americans, Native Hawaiians, and Pacific Islanders. The Office is also encouraged to focus on existing and developing areas of culturally appropriate research that seeks to reduce the risk of contracting HIV through high-risk behaviors and the transmission of HIV infection in the targeted minority populations. (Page 106)

Action taken or to be taken

OAR is directing increased resources toward research to develop new interventions that will have the greatest impact on these groups. These include interventions that address the co-occurrence of other sexually transmitted diseases, hepatitis, drug abuse, and mental illness; and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities. NIH is making significant investments to improve research infrastructure and training opportunities for minorities and will continue to assure the participation of minorities in AIDS clinical trials, as well as in natural history, epidemiologic, and prevention studies. NIH has provided additional funds to projects aimed at increasing the number of minority investigators conducting behavioral and clinical research; targeting the links between substance abuse, sexual behaviors, and HIV infection; increasing outreach education programs targeting minority physicians and at-risk populations; and expanding the portfolio of population-based research. One of these projects is a series of Training and Career Development Workshops for racial and ethnic minority investigators. These workshops provide minority investigators with an opportunity to learn more about available NIH funding mechanisms and to meet and network with

senior minority investigators who receive significant levels of NIH funding.

OAR has directed funds to the NIH ICs to support a broad array of behavioral intervention studies with specific focus on African American populations. These studies are characterizing the disease process in drug users, factors influencing disease progression, consequences of multiple co-infections, effectiveness of therapeutic regimens, and the impact of health care access and adherence to therapeutic regimens on disease outcomes. The increasing number of AIDS cases among minorities in the U.S. underscores the importance of research to define and utilize cultural, social, and contextual factors that affect HIV risk behaviors. The role of alcohol and drug use in facilitating HIV transmission through social networks in all communities also is being explored within these social frameworks.

OAR sponsors regional workshops targeted to Hispanic, Native American, Asian and Pacific Islanders, and African American communities. Events have focused on issues relating to women, children, and injecting drug users. These meetings provide a forum for the presentation of research information. To ensure that the meetings are culturally appropriate and effective, they are planned in collaboration with scientists, researchers, community leaders, people living with HIV/AIDS, and care providers in the community. OAR is collaborating with the Indian Health Service and other HHS agencies to plan a national conference in Spring 2006 on HIV/AIDS in Native Americans, Alaska Natives, Hawaiian Natives, and Pacific Islanders.

FY 2005 Senate Appropriations Committee Report Language (S. Rpt. 108 - 345)

Microbicides for the Prevention of HIV - Microbicides, a class of products that would be applied topically to prevent HIV, represent a promising prevention strategy, with the potential to be especially significant in preventing HIV in women, who now account for more than half of the individuals newly infected with HIV globally. Once developed, microbicides and vaccines would serve as complementary HIV prevention technologies. NIH, principally through NIAID, spends the majority of Federal dollars in this area. The Committee remains concerned that microbicide research at NIH is currently conducted with no single line of administrative accountability or specific funding coordination. The Director of NIH, in consultation with OAR and in coordination with NIAID, NICHD, NIDA, NIMH, and ORWH, is urged to establish a microbicides branch or comparable dedicated unit specifically for microbicides research and development, with appropriate staff and funding.

Action taken or to be taken

The Office of AIDS Research (OAR), located in the Office of the Director, NIH, was established as the lead office to coordinate microbicide research among the NIH institutes and with other Federal agencies, providing a single line of administrative accountability and specific funding coordination. OAR plans, coordinates, and develops a trans-NIH budget for all NIH AIDS research, including microbicide research. OAR has carried out its mandate and worked to accelerate this important field of research. In 2001, OAR developed the first *NIH Strategic Plan for Microbicides,* in parallel with the annual *NIH Plan for HIV-Related Research,* which establishes the scientific agenda for the conduct of NIH ATDS-related research. The Plan has been updated every year to reflect the most recent scientific advances and priorities in microbicide research. NIH staff and non-government experts, including other DHHS agencies (CDC, FDA) and other U.S. government agencies (USAID) work together to develop the plan.

OAR provides funding oversight by developing an annual trans-NIH budget and allocating all appropriated AIDS research funds to the Institutes, based explicitly on the priorities and objectives of the strategic plan. The ICs submit their AIDS-related research budget requests to OAR based on the plan's priorities and objectives. OAR allocates the AIDS research budget levels to each IC. The allocation is based on the scientific priority of the proposed initiatives in relation to the Plan and to other IC submissions to eliminate redundancy and/or to assure cross-Institute collaboration. OAR consults regularly with the IC Directors and maintains knowledge of the ongoing microbicide portfolios supported by each IC. This funding coordination process ensures that NIH AIDS-related research funds will be provided to the most compelling scientific opportunities.

OAR established the Trans-NIH Microbicide Research Working Group, comprised of representatives from NIAID, NIDA, NICHD, NIMH, FIC, and ORWH, to facilitate information sharing about ongoing and planned initiatives; facilitate collaborative research; and develop the annual strategic plan for microbides. OAR also developed the first *U.S. Government Strategic Plan for Microbicides* in coordination with CDC, FDA, and USAID. This Plan identifies the scientific agenda in microbicide research and summarizes each agency's current activities.

NIH believes that the planning, priority setting, funding coordination, and administrative oversight provided by OAR, along with the collaborative activities of the trans-NIH Microbicide Research Working Group represent the most effective and efficient approach to carrying out the complementary, multidisciplinary and multi-institute microbicide research and development agenda.