

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2005 Budget Request

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Jack Whitescarver, Ph.D.
Director, Office of AIDS Research

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William Beldon, Acting Deputy Assistant Secretary for Budget, HHS
Kerry N. Weems, Acting Assistant Secretary for Budget, Technology and Finance, HHS

Mr. Chairman and Members of the Committee, I am pleased to present the President's budget request for the AIDS research programs of the NIH for Fiscal Year 2005, a sum of \$2,930,397,000 an increase of \$80,445,000 above the comparable FY 2004 appropriation.

The NIH represents the largest and most significant public investment in AIDS research in the world – a comprehensive program of basic, clinical, and behavioral research on HIV infection and its associated opportunistic infections and malignancies. Perhaps no other disease so thoroughly transcends every area of clinical medicine and scientific investigation, crossing the boundaries of the NIH institutes. The Office of AIDS Research (OAR) plays a unique role at the NIH. OAR coordinates the scientific, budgetary, and policy elements of the NIH AIDS program, supported by nearly every Institute and Center; prepares an annual comprehensive trans-NIH plan and budget for all NIH-sponsored AIDS research; facilitates NIH involvement in international AIDS research activities; and identifies and facilitates scientific programs for multi-institute participation in priority areas of research.

WORLDWIDE PANDEMIC

AIDS is the deadliest epidemic of our time. More than 22 million people have already died of AIDS – 3 million of them in 2003 alone – the largest number ever. 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.¹ 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."² According to a UN report, "The epidemic has not only killed people; it has imposed a heavy burden on families, communities and economies. The misery and devastation already caused by HIV/AIDS

is enormous, but it is likely that the future impact will be even greater...The HIV/AIDS epidemic has erased decades of progress in combating mortality and has seriously compromised the living conditions of current and future generations. 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.” The report also highlights “the long-term damage accruing to human capital, as children’s education, nutrition and health suffer directly and indirectly as a consequence of HIV/AIDS. The effects of lowered investment in the human capital of the younger generation will affect economic performance for decades to come, well beyond the timeframe of most economic analysis.”³ Another dimension to the epidemic in Africa was cited in the *New York Times*: “As a result of HIV, the worst-hit African countries have undergone a social breakdown that is now reaching a new level: African societies’ capacity to resist famine is fast eroding. Hunger and disease have begun reinforcing each other.”⁴

A recent CIA report estimated that by 2010, five countries of strategic importance to the U.S. – Nigeria, Ethiopia, Russia, India, and China – collectively will have the largest number of HIV/AIDS cases on earth.⁵ *Foreign Affairs* magazine stated: “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 Eurasia – and thus in the relationship between Eurasian states and the rest of the world.”⁶ Dramatic increases in HIV infection also are occurring in Eastern Europe, Central Asia, Latin America, and the Caribbean.

THE U.S. EPIDEMIC

According to CDC, the decline in death rates observed in the late 1990s, due largely to expanded use of new antiretroviral therapies (ART) that prevent progression of HIV infection to AIDS, has now leveled off; and AIDS incidence increased 2 percent in 2002 (over 2001). This means that the overall epidemic is continuing to expand.^{7 8 9} In addition, use of ART has now been 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.¹⁰ The appearance of multi-drug resistant strains of HIV presents an additional serious public health concern.^{11 12 13 14 15} According to CDC reports, approximately one quarter of the HIV-infected population in the United States also is infected with hepatitis C virus (HCV). HIV/HCV 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.¹⁶ This expanding and evolving U.S. epidemic presents new and complex scientific challenges.

COMPREHENSIVE AIDS RESEARCH PLAN AND BUDGET

To address these compelling scientific questions, the OAR develops an annual comprehensive trans-NIH AIDS research plan and budget, based on the scientific priorities and opportunities that will lead to better therapies and prevention strategies for HIV infection and AIDS. The planning process is inclusive and collaborative, involving the NIH Institutes, as well as eminent non-government experts from academia, industry, foundations, and AIDS community representatives. The Plan serves as the framework for developing the annual AIDS research budget for each Institute and Center, for determining the use of AIDS-designated dollars, and for tracking and monitoring those expenditures. The planning process also serves to monitor and assess scientific progress on an annual basis.

The Plan establishes the NIH AIDS scientific agenda in the areas of: Natural History and Epidemiology; Etiology and Pathogenesis; Therapeutics; Vaccines; and Behavioral and Social Science. In addition, the plan addresses the cross-cutting areas of: Microbicides; Racial and Ethnic Minorities; Women and Girls; Prevention Science; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination. In consultation with the Director of NIH, the OAR determines the total annual 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, at each step of the budget development process up to the Conference Committee. To accomplish this, OAR consults regularly with the Institute and Center Directors. This process allows the OAR to ensure that NIH AIDS research funds will be provided to the most compelling scientific opportunities, rather than a distribution based solely on a formula.

OAR plays a crucial role in identifying scientific areas that require focused attention and facilitating multi-Institute activities to address those needs. OAR fosters this research through a number of mechanisms, such as designating funds and supplements to jump-start or pilot program areas, sponsoring workshops or conferences to highlight a particular research topic, and sponsoring reviews or evaluations of research program areas to identify research needs.

The overarching priorities that continue to frame the NIH AIDS research agenda are: prevention research to reduce HIV transmission, including development of vaccines, microbicides, and behavioral interventions; therapeutics research to develop simpler, less toxic, and cheaper drugs and drug regimens to treat HIV infection and its associated illnesses, malignancies, and other complications; international research, particularly to address the critical needs in developing countries; and research targeting the disproportionate impact of AIDS on minority populations in the United States. All

of these efforts require a strong foundation of basic science, the bedrock of our research endeavor.

NEW CHALLENGES IN THERAPEUTICS RESEARCH

While multiple ART drug combinations continue to successfully reduce viral load and restore immune responses in many HIV-infected individuals, these regimens also can result in serious toxicities and side effects, single- and multiple drug-resistance, and other complications that make them unacceptable for some individuals. These side effects and complications appear to be increasing as HIV-infected individuals continue on drug regimens. More deaths occurring from liver failure, kidney disease, and cardiovascular complications are being observed in this patient population. NIH-sponsored research efforts continue to develop better antiretroviral drugs and treatment regimens that demonstrate less toxicity, activity in viral and cellular reservoirs, reduced development of drug resistant virus, improved pharmacodynamics and pharmacokinetics, easier compliance, and lower cost.

While the incidence of certain opportunistic infections (OIs) and malignancies has decreased with the advent of ART, the number of cases of TB, multiple drug resistant TB, and other coinfections such as Hepatitis B virus and Hepatitis C virus has increased. The development of practical and affordable treatment regimens against HIV coinfections and endemic diseases in developed and developing nations is an NIH priority.

PREVENTION RESEARCH

NIH supports a comprehensive approach to HIV prevention research that includes contributions from the biomedical, behavioral, and social sciences. Our biomedical prevention research priorities include the development of vaccines, topical microbicides, strategies to prevent mother-to-child transmission – including a better understanding of risk associated with breast-feeding – and management of sexually

transmitted diseases (STDs). NIH also supports behavioral research strategies, including interventions related to drug and alcohol use. Efforts continue to identify the most appropriate intervention strategies for different populations and sub-epidemics in the U.S. and around the world. As a result of increased NIH funding, many new approaches to HIV vaccines are being pursued. Although production of candidate vaccines for clinical study has proceeded slowly, approximately 14 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, located on the NIH campus, recently launched the first Phase I clinical trial of a multi-clade, multi-gene vaccine candidate.

INTERNATIONAL RESEARCH

NIH bears a unique responsibility to address the urgency of the global AIDS epidemic. To meet that need, the OAR established an initiative and strategic plan for global research on HIV/AIDS and has significantly increased research efforts in the past several years to benefit resource- and infrastructure-poor nations. NIH supports a growing portfolio of research conducted in collaboration with investigators in developing countries. Results of this research benefit the people in the country where the research is conducted, as well as people affected by HIV/AIDS worldwide. Critical to the success of these international studies are foreign scientists who are full and equal partners in the design and conduct of collaborative studies. To that end, NIH also supports international training programs and initiatives that help build infrastructure and laboratory capacity in developing countries where the research is conducted.

WOMEN AND MINORITIES

Women experience HIV/AIDS differently from men. NIH research has demonstrated that women progress to AIDS at lower viral load levels and higher CD4 counts than men. Women also experience different clinical manifestations and

complications of HIV disease. These findings may have implications for care and treatment of HIV-infected women, particularly with ART. There are many research questions that remain unanswered about specific characteristics of women and girls that might play a role in transmission, acquisition, or resistance to HIV infection during different stages of the life course.

In many U.S. urban centers, HIV seroprevalence rates mimic those found in some developing nations. These findings, along with the resurgence of STDs and associated high-risk behaviors, demonstrate the need for comprehensive strategies to decrease HIV transmission in affected vulnerable populations, and improve treatment options and treatment outcomes. OAR is directing increased resources toward research to develop new interventions that will have significant 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 ensure the participation of minorities in AIDS clinical trials, as well as in natural history, epidemiologic, and prevention studies.

SUMMARY

The human and economic toll of the AIDS pandemic is profound, demanding a unique response that is complex, comprehensive, multi-disciplinary, and global. The NIH role in this response is fundamental and unprecedented. The nation's investment in AIDS research is reaping even greater dividends, as AIDS-related research is unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases. The authorities of the OAR allow NIH to pursue a united research front against the global AIDS epidemic. We are deeply grateful for

the continued support the Administration and this Committee have provided to our efforts.

Footnotes

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7. CDC Year-End HIV/AIDS Surveillance Report for 2002 (CDC, 2003).
8. "Centers for Disease Control and Prevention HIV Prevention Strategic Plan Through 2005," (CDC, 2001).
9. "HIV/AIDS Update – A Glance at the HIV Epidemic," (CDC, 2001).
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14. M. Waldholz, "Drug Resistant HIV Becomes More Widespread," *Wall Street Journal*, 2/5/99.
15. "World Health Report on Infectious Diseases: Overcoming Antimicrobial Resistance," (WHO, Geneva, 2000).
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