NATIONAL INSTITUTES OF HEALTH

FISCAL YEAR 2003

PLAN FOR HIV-RELATED RESEARCH

XI: INTERNATIONAL RESEARCH

PREPARED BY THE OFFICE OF AIDS RESEARCH

AREA OF EMPHASIS:

International Research

SCIENTIFIC ISSUES

AIDS continues its devastating march. The Joint United Nations Programme on HIV/AIDS (UNAIDS) notes in its report, "AIDS Epidemic Update: December 2000," that the pandemic now is worse than predicted a decade ago. The impact of AIDS on developing nations of Africa, Asia, Europe, and Latin America is staggering, with even greater potential disaster to come. The cost in lost productivity and profitability, sickness and death, and a significant reduction in the skilled workforce in developing countries will have major economic impact. In South Africa, for example, the epidemic is projected to reduce the economic growth rate by 0.3–0.4 percent annually, resulting in a gross domestic product 17 percent lower than it would have been without the influence of the AIDS epidemic.

According to data released by UNAIDS:

- Over 36 million people are living with HIV/AIDS worldwide;
- Nearly 22 million have died of AIDS thus far in the epidemic; and
- Approximately 5.8 million were newly infected with HIV in 2000.

As home to 70 percent of the adults and 80 percent of the children in the world living with HIV, Africa is the region most severely affected. While encouraging signs suggest that the epidemics in sub-Saharan Africa may be stabilizing, the explosion of new infections in countries that have had low rates could reverse this trend. Epidemics, unfortunately, are rapidly

escalating in other areas of the world as well. In Eastern Europe and the former Soviet Union, the number of people estimated to be living with HIV/AIDS has increased from 420 at the end of 1999 to an estimated 7,000 by the end of 2000, with new epidemics emerging in Uzbekistan and in Estonia. The potential for massive epidemics in China and Vietnam is of major concern, as is the course of the established epidemic in India. Indonesia, which for many years has not seen an escalation of new infections, has reported an increase in prevalence of HIV among sex workers from 6 to 26 percent. Rates of HIV are higher in the Caribbean and Central America than in other areas of Latin America, although Brazil and Guyana are experiencing significant epidemics. Haiti remains the most affected nation in the Caribbean, with 13 percent of pregnant women found to be HIV positive. Other countries in the region with high rates include Belize, Guatemala, and Honduras in Central America, and the Bahamas, Dominican Republic, and Trinidad and Tobago in the Caribbean.

Research to address the global pandemic is essential. Since the early days of the epidemic, NIH has supported research efforts in countries impacted 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, NIH has maintained a strong international research portfolio. Development of a research infrastructure, including training of scientists and health care providers, is an essential adjunct to these research programs. NIH has expanded its research effort to encompass more than 50 countries around the world, and collaborations between scientists in the United States and in developing countries have provided much valuable information. Results of this research benefit not only the people in countries where the research is conducted, but people affected by HIV/AIDS worldwide.

This research portfolio continues to grow and evolve in response to the continuing pandemic. In 2000, the Office of AIDS Research established a new initiative and plan for global research on HIV/AIDS. The plan was included as part of the FY 2002 NIH Plan for HIV-Related Research and has now become part of the annual AIDS planning process. To meet the goals of this initiative, OAR established the NIH Global AIDS Research Strategy Group, a high-level working group comprising top officials of NIH and representatives from other governmental agencies. In addition, NIH collaborates with UNAIDS, the World Health Organization, host country governments, foundations, and nongovernmental organizations, as well as in-country scientists in the planning and implementation of the international AIDS research portfolio.

This section of the Plan highlights NIH efforts to address the global pandemic through research and related infrastructure development. These activities also are described in the relevant Areas of Emphasis throughout the Plan.

INFRASTRUCTURE FOR CLINICAL TRIALS OF NEW INTERVENTIONS

PRIORITY FOR FUTURE RESEARCH:

- **Develop in-country infrastructure for the conduct of clinical trials of therapeutic and prevention interventions, including the use of antiretroviral therapy (ART), therapies for opportunistic infections (OIs), vaccines, microbicides, other biomedical and behavioral strategies to prevent sexual transmission, and interventions to prevent mother-to-child transmission.**

There is a pressing need in resource-poor countries for culturally appropriate and effective interventions to prevent transmission of HIV and to treat HIV and associated complications. From a global perspective, the major modes of acquiring HIV infection are heterosexual transmission and injecting drug use, with the vast majority of infections occurring through sexual transmission. Biomedical and behavioral interventions to curb this transmission in very diverse settings are urgently needed. With women comprising more than 47 percent of adults infected with HIV worldwide, preventing transmission from an infected mother to her child is a significant challenge, particularly in resource-poor settings of the world. Therapeutic strategies are needed for treatment of HIV with ART, prophylaxis, and treatment of OIs, other sexually transmitted diseases (STDs), malignancies, and neurological conditions.

Various sections of the Plan describe NIH efforts to develop vaccines for HIV; 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 drug and alcohol use; drug and non-drug strategies to prevent mother-to-child transmission; therapeutics for OIs and other conditions; and approaches to using ART in resource-poor settings. But before prevention and treatment interventions can be implemented in different geographic settings, their safety and efficacy must be demonstrated in such settings through clinical trials and other intervention research. However, in resource-poor countries, adequate infrastructure may not exist to conduct such trials, and it must be developed. Specific infrastructure needs include (1) developing research sites through establishment of 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; and (3) transferring appropriate clinical and laboratory technologies. Critical to this effort is the need to devise innovative funding mechanisms and approaches.

USE OF ANTIRETROVIRAL THERAPY

PRIORITY FOR FUTURE RESEARCH:

- **Facilitate the rapid initiation of studies of the use of ART in resource-limited settings through: (1) training developing country clinicians and scientists; (2) strengthening in-country laboratory capacity; (3) developing low cost alternatives to viral load and CD4+ cell counts for monitoring treatment efficacy and toxicity; (4) creating innovative funding approaches; and (5) establishing early dialogue with industry**.

The use of regimens of ART has extended the length and improved the quality of life for many HIV-infected people in industrialized countries. Unfortunately, these therapies have not been widely utilized in resource-poor nations due to factors of cost and the need for an adequate health care infrastructure to administer and monitor complex therapeutic regimens of toxic agents. However, in 2001, momentum has grown to provide options for the use ART in these regions. It is therefore critical to move rapidly to investigate the safety and efficacy of various ART regimens in diverse resource-poor settings. For example, differences in diet or the use of medications for endemic diseases may alter the toxicity or the efficacy of antiretroviral drugs, as compared with industrialized areas, and such information is urgently needed as the world progresses to more widely implement ART.

In order to move rapidly in this field, the laboratory and human resource infrastructure already established in the developing world needs to be further developed specifically for treatment research, including training of in-country scientists, clinicians, and other health care workers. Low cost approaches that can be used effectively in these settings to monitor patients for treatment efficacy and toxicity will need to be developed, with emphasis on alternatives for using viral load and CD4+ cell counts. The need to move rapidly also will require the use of creative and flexible funding mechanisms. Finally, it is critical that dialogue is initiated early with the pharmaceutical industry concerning the provision of drugs both for the research effort and once treatment regimens have been demonstrated to be safe and efficacious.

HIV-RELATED ILLNESS IN DIVERSE GEOGRAPHIC SETTINGS

PRIORITY FOR FUTURE RESEARCH:

- **Define the spectrum of HIV-related illness relative to diverse geographic settings, including OIs and those conditions that emerge as a consequence of ART and longer survival.**

Since the beginning of the epidemic in the United States, research has been conducted to characterize a variety of OIs, cancers, and other conditions that have been shown to be associated with HIV infection. Methods for diagnosis, prevention, and treatment of these conditions have been developed. More recently, the extensive use of effective ART has resulted in a dramatic decrease in many of these conditions. In the developing world, such conditions remain the cause of morbidity and mortality associated with HIV infection. It is necessary to develop vaccines and drugs to prevent and treat them, particularly since antiretroviral drugs are only beginning to be used in these settings and may not be widely used for some time. As a foundation for the development of such interventions, it is essential to characterize the nature, prevalence, and course of disease of OIs, as well as other HIV-related illnesses found in diverse geographic settings. An integral component is development of diagnostic methods to detect these illnesses. The HIV-related global epidemic of tuberculosis is well documented. However, little is known about other OIs and conditions. It might be expected that the occurrence of conditions varies greatly depending on geography as, for example, fungal infections might prevail in one setting and bacterial infections in another. The background presence of specific cancers might affect the pattern of HIV-related cancers. Diseases not found in the developed world may be important in some regions. For example, it has been demonstrated that a fungal infection due to *P. marnefii* is a significant OI in Thailand, where scientists have now developed an effective treatment for it.

At the same time, in the United States, extended survival has been associated with the development of new conditions, some of which result from the treatment itself. As use of ART increases in the developing world, it will be necessary to characterize conditions that emerge in these settings, since factors such as diet, the presence of endemic diseases, and the use of drugs to treat them may affect the nature and occurrence of such conditions.

DRUG AND ALCOHOL USE

PRIORITY FOR FUTURE RESEARCH:

- **Support studies addressing drug and alcohol use and risk of transmitting and acquiring HIV infection, including transition between noninjection and injection drug use, drug addiction treatment strategies, and the relationship between alcohol use and sexual risk behaviors**.

UNAIDS reports that injecting drug use is a growing factor in the AIDS epidemic, estimating that about 10 percent of HIV infections globally result from injecting drug use. It is fueling epidemics in Central and Eastern Europe and countries of South and Southeast Asia, where in some countries, more than half of HIV infections are attributed to injecting drug use. As a social phenomenon, injecting drug use itself is reported to be growing in all regions of the world, including Africa. Thus the potential exists for drug-related epidemics to arise in new places, as well as for established epidemics to escalate.

Injecting drug users who share needles and other contaminated equipment are at high risk of acquiring or transmitting HIV. However, the use of noninjecting drugs, including alcohol, also is associated with increased risk, particularly through associated sexual behavior. Of great concern is the use of alcohol and other drugs among young people. As the most widely used drug in the world, alcohol use is associated with increased risky sexual behavior in many types of social situations, and thus with the spread of HIV in a variety of social contexts. In many parts of the world, drug users are more likely to be involved in the sex industry, greatly enhancing their risk of infection and the chances of HIV spreading even wider in the community. Injecting drug users are particularly vulnerable to HIV and AIDS because they are often also poor and marginalized. Culturally relevant interventions are needed at all levels—individual, social network, community, and society—to prevent this mode of transmission.

ETHICAL CHALLENGES

PRIORITY FOR FUTURE RESEARCH:

- **Address ethical challenges in research in resource-poor settings, including developing in-country human subjects review committees; ensure a leadership role for in-country investigators in the countries where studies take place.**

Ethical considerations must be paramount in the development of international collaborations and NIH support of research activities in other countries. It is universally accepted that researchers should adhere to and address standard ethical principles in the design and conduct of research. Essential to the protection of human subjects participating in research,

these principles are outlined in several documents and include respect for persons, beneficence, and justice. However, the vastly different economic and cultural contexts in which research is conducted in international settings create many challenges for researchers and funding agencies in the application of these principles. For example, obtaining voluntary informed consent from each study participant may be complicated in some settings by social customs requiring the involvement of others in the community in this process, such as family members or community leaders. Differences in law, regulation, and public policy, as well as organizational structures, mean that careful consideration must be given to how ethical standards of both the United States and the country where research is conducted can met. It is essential that proposed studies receive full ethical review and approval in the country where the research will be conducted, as well as in the United States. Unfortunately, many resource-poor nations do not have mechanisms in place to conduct ethical review. Thus, a critical component of research infrastructure is strengthening the capability of countries to conduct their own independent ethical review of research.

Integral to addressing ethical considerations is ensuring a leadership role for foreign scientists in the countries where studies are conducted. In development of collaborations, they must be full and equal partners in the design and conduct of studies and have full responsibility for the conduct of studies in-country. This responsibility should include full participation in the conceptualization of the research; development of protocols; study implementation and collection of data; data processing and analysis; and dissemination of information about the research and its results, through the press, professional meetings, and publications in scientific journals.

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE:

Build research capacity in international settings that will: (1) provide an environment that promotes the development of equal partnerships between U.S. and foreign investigators; (2) facilitate the conduct of basic biomedical and behavioral research and long-term cohort studies; (3) serve as loci for studies of safety and efficacy of biomedical and behavioral prevention interventions (including Phase I, II, and III trials of vaccines, microbicides, and therapies); (4) function as training sites for investigators from throughout the region; and (5) serve as bridges with programs that provide services.

STRATEGIES:

Site Development

- Develop new and existing international research sites as rapidly as possible, addressing geographic regions and specific populations where HIV is and/or will be a major cause of morbidity and mortality.
- Build capacity to enable the conduct of basic and applied research, clinical trials, and studies of clinical aspects of HIV and related conditions, with emphasis on good clinical practices of the intensity and rigor needed for large-scale trials by:
  - conducting incidence assessments;
  - enhancing laboratory capacity;
  - developing clinical capabilities;
  - improving capacity for voluntary counseling and testing;
  - enhancing data collection and analysis capabilities;
  - developing strategies for recruitment of participants into treatment and prevention studies;
  - developing strategies for maintaining adherence and follow-up of study participants; and
  - enhancing the ability to assure protection for human subjects involved in research and the ethical conduct of research.
- Conduct studies of incidence and feasibility at 100 international sites in order to identify at least 60 sites suitable for the conduct of efficacy trials of HIV prevention interventions.

Training

- Continue to support training of clinicians and scientists from developing nations to enhance the conduct of research on HIV and AIDS, including training in clinical aspects; treatment and care (e.g., clinical trials of therapeutic strategies for HIV and opportunistic infections [OIs]); development and testing of vaccine candidates; impact of alcohol and other substance abuse/dependence on HIV transmission and disease progression and other biomedical and behavioral prevention research.
- Develop in-country training partnerships and support "south-to-south" training to enable trained investigators returning to their home countries to serve as training resources for other scientists in their own countries and geographic regions.
- Support training in ethical issues related to the conduct of research.
- Ensure training that specifically includes the requirements of "good clinical practices."
- Provide training to ensure clinicians and other health care workers understand infection control principles and can implement proper procedures in resource-poor settings.
- Expand training to address research administration, fiscal accountability, research support services, and grants management.
- Enhance training to develop clinical capability and to facilitate technology transfer, including the delivery of antiretroviral therapy (ART).

Collaboration and Coordination

- Encourage the continued development of collaborations between in-country and U.S. investigators to maximize the research effort in resource-limited settings.
- Ensure the leadership role of in-country investigators in countries where studies take place by involving them in all stages of the research, including conceptualization of the research question, study design, development of protocols, study implementation and collection of data, data analysis, publication and presentation of research results, and interaction with the media.

- Provide assistance to foreign collaborators in addressing regulatory issues and special oversight mechanisms.
- Enhance coordination of NIH international research efforts.
- Coordinate NIH AIDS and non-AIDS research efforts, particularly where projects are active in the same country and/or region.
- Work with other U.S. governmental agencies, foreign Governments, international organizations, nongovernmental organizations (NGOs), and industry to facilitate development and testing of vaccines, microbicides, drugs, and other prevention strategies, including behavioral interventions, and to ensure that effective interventions resulting from research are available to study participants and host-country populations after completion of the research.
- Explore collaboration with traditional healers to facilitate accomplishment of research objectives, including enhancing the participation of indigenous populations in research and improving understanding of the complex context of addressing diseases in diverse geographical settings.
- Develop programs to enhance reporting of AIDS issues relative to geographical areas heavily impacted by the pandemic by (1) strengthening the skills of in-country and U.S. scientists in communicating effectively to the media and (2) preparing the media in such countries to report on health issues.

Ethical Issues

- Enhance the capability of foreign institutions to conduct independent ethical and scientific review.
- Encourage the participation of local communities, NGOs, and Governments in the development of research protocols.
- Address ethical challenges in both research and the implementation of research results in resource-limited settings.
- Consider the need for study participants and their communities in host countries to have maximum possible access to any preventive or therapeutic products developed during the research, and initiate dialogue with pharmaceutical companies early in the process of planning for clinical trials in resource-limited settings.

- Ensure confidentiality of information about substance abusers, including information on individuals in treatment for substance use.
- Conduct research designed to identify ways to improve the application of ethical principles in the conduct of research.

Technology Transfer

- Transfer clinical and laboratory technologies that may be sustained and used for implementation of prevention, symptom management, and patient care programs once research studies are completed.
- Enhance the translation of research results to improve patient management, develop prevention programs appropriate to the setting, and effect policy changes in resource-poor settings around the world.
- Integrate operational and health services research with clinical research to facilitate the translation of research findings into clinical practice and public health programs.
- Provide improved access to information through enhanced information technology.
- Identify logistical issues that need to be addressed to accomplish effective, wide-spread delivery of ART, HIV vaccines, microbicides, and other products.

Funding Mechanisms

- Develop creative and innovative approaches and mechanisms to provide funding for infrastructure development and for rapidly launching clinical trials, including improvement of space for confidential counseling, clinical care, and laboratory investigations.
- Design flexible and rapid mechanisms to permit conduct of expanded prevention clinical trials when preliminary studies indicate that a product or approach merits full-scale evaluation.
- Continue to explore new funding approaches for international research, including direct funding of overseas investigators and provision of indirect costs to foreign institutions.

OBJECTIVE:

Establish the most effective, affordable, and practical ways to care for HIV-infected adults, adolescents, and children in resource-limited settings, including treatment of HIV and related conditions, such as OIs, malignancies, other sexually transmitted diseases (STDs), and neurological conditions.

STRATEGIES:

Treatment of HIV with Sustainable Antiretroviral Therapy

- Determine safe and effective ART regimens, including timing of initiation and appropriate drugs, that can be used in diverse resource-poor geographic settings.
- Investigate the impact of co-infection with other endemic diseases on the use of ART.
- Study drug-drug interactions among antiretroviral drugs, medications for other endemic diseases, and medications or substances used for nonmedical reasons.
- Assess the impact of nutritional status and nutritional interventions on patient survival and efficacy and tolerability of ART.
- Determine the efficacy of ART regimens on various clades prevalent around the world.
- Examine the potential use of HIV vaccines in the context of suppressive ART.
- Develop and evaluate suitable, sustainable approaches for monitoring treatment efficacy, side effects, and toxicity, with particular emphasis on alternatives for current high-cost CD4+ cell counts and HIV load methodologies.
- Determine the impact of ART on development of drug-resistant strains of HIV in diverse geographical setting.
- Assess the impact of ART on HIV transmission and community prevalence.
- Determine the social, psychological, societal, and economic impact of ART on individuals, families, and communities, including impact on personal risk behavior.

- Examine the effectiveness of various approaches to administration (e.g., directly observed therapy or directly delivered therapy).
- Develop culturally appropriate mechanisms to identify persons eligible for treatment and to overcome factors such as stigma, which can limit the provision of treatment and care.
- Develop strategies to ensure that prevention efforts in resource-limited countries are simultaneously preserved and enhanced when clinical trials and later ART treatment programs are established.

Sustainable Strategies for Preventing and Treating OIs and Other HIV-Related Conditions

- Develop simplified diagnostic tests for OIs.
- Investigate sustainable strategies for preventing, treating, and monitoring response to treatment of OIs and other HIV-related conditions.
- Assess the impact of available antibiotic treatment and prophylaxis regimens to optimize therapeutic approaches for tuberculosis and other OIs.
- Study drug-drug interactions with drugs used to prevent and treat endemic infections.
- Develop simple clinical algorithms for guiding initiation of prevention or treatment of infections.
- Identify affordable means to target high-risk patients for initiation of prophylaxis.
- Develop methods to monitor development of antimicrobial resistance by HIV-related and endemic pathogens infecting both study participants and the general population.
- Identify strategies to limit development of drug resistance.
- Develop strategies to enhance and monitor adherence to therapy/prophylaxis for OIs.
- Determine the safety and effectiveness of available immunizations in diverse populations.

- Assess the burden of tuberculosis and the relative importance of reactivation versus *de novo* infection in various settings.

Approaches to Care

- Continue to identify better, low-cost alternatives for diagnosis of HIV infection.
- Develop better approaches to voluntary counseling and testing that encourage knowledge of one's status and help mitigate social harm.
- Identify clinical management approaches, including effective palliative care strategies, and overall care needs among HIV-infected persons in diverse settings.
- Develop care models that integrate HIV/AIDS care into existing programs, such as tuberculosis control programs and alcohol and other substance abuse/dependence treatment programs, to avoid duplication of efforts.
- Develop approaches to HIV prevention education suitable for use in HIV care settings.
- Develop tuberculosis prevention and education strategies for use with HIV-infected individuals, as well as the general population.
- Develop interventions to mitigate the negative social consequences of HIV infection, including AIDS stigma, particularly among AIDS orphans.

OBJECTIVE:

Develop and evaluate biomedical and behavioral prevention interventions appropriate for use in diverse geographical settings.

STRATEGIES

Blood-Borne Transmission

- Develop strategies to prevent blood-borne transmission in health care settings, including recruitment and retention of appropriate blood donors, pre-donation counseling of all blood donors, blood screening strategies and technologies, those that address use/misuse of transfusion and injections, and the implementation of universal precautions.

Sexual Transmission

- Develop biomedical strategies to prevent sexual transmission of HIV, with particular emphasis on women and adolescents, including microbicide development, studies of barrier methods and factors affecting their use, and syndromic management of STDs.
- Establish the most effective and sustainable ways to change or prevent sexual and other behaviors such as rape and commercial sex work that foster the spread of HIV in resource-limited settings.
- Investigate the effectiveness of community-based and community-level HIV prevention programs, including abstinence-based education, and develop strategies to replicate and extend the effective elements.

Substance Use

- Conduct studies to identify sustainable interventions at the level of the individual, social network, community, and society to prevent HIV transmission as a result of alcohol and other drug use or addictive behavior.
- Evaluate innovative, culturally relevant, contextually appropriate substance use treatment programs for their utility as HIV prevention approaches in different international settings.
- Determine the factors involved in social networks of injection and non-injection drug users that influence the speed and patterns of diffusion of HIV infection and design prevention programs based on the results.

Mother-to-Child Transmission

- Further identify cost-effective drug and non-drug regimens for preventing mother-to-child transmission (MCT), including research on infant feeding and treatment of reproductive tract infections.
- Examine the role of maternal and infant nutrition during the peripartum and postpartum periods in reducing morbidity and mortality in infected mothers and their infants and in reducing MCT of HIV.

Vaccine Development

- Continue the accelerated efforts toward development of vaccine candidates suitable for use around the world, including expanded Phase III clinical trials in international settings.
- Examine relevant behavioral issues related to the conduct of vaccines research and acceptability.

Cross-Cutting Strategies

- Develop sustainable, behavioral, economic, and environmental interventions to address the multiple risk factors present in selected populations.
- Conduct multidisciplinary prevention research in multiple settings, including medical treatment and community support and care organizations, based on rapid assessments of at-risk groups identified in each local geographic context.
- Conduct research to integrate the multiple components of diverse issues of sexuality, alcohol and other substance use, and mental health into HIV prevention programs.
- Encourage research on the impact of integration of prevention and care services at the public health level, including evaluation, dissemination, and expansion of model programs.
- Develop new approaches to voluntary counseling and testing and assess them for cost-effectiveness and impact on reducing risk from sexual behavior and drug use in settings with varying levels of seroprevalence.
- Evaluate strategies to reduce stigma and increase willingness of individuals to (1) enter into voluntary counseling and testing, (2) undertake infant feeding approaches that do not conform to the social norm, and (3) enter antiretroviral therapy.

- Prepare for 10 major Phase III efficacy trials that will include resource-limited settings to evaluate HIV prevention interventions, including vaccines, therapeutics, chemical and physical barriers, control of STDs and other reproductive tract infections, interventions to address alcohol and other drug abuse/dependence and treatment, and other behavioral interventions, and new strategies to prevent MCT of HIV.
- Conduct translational research in areas such as syndromic management of STDs, implementation of nevirapine for MCT, and breast-feeding practices.

OBJECTIVE:

Conduct population-based studies relevant to the geographic areas of the world and specific populations hardest hit by the epidemic.

STRATEGIES:

- Utilize population-based studies to examine basic scientific questions about HIV, its transmission, and host response, including viral evolution, viral diversity, and human immunology.
- Identify biological determinants of infectiousness and susceptability to infection, including both viral and host factors.
- Study gender-related biological factors affecting susceptability to infection, including the use of hormonal contraceptives and the presence of gender-specific conditions such as human papillomavirus and cervical cancer.
- Study gender-related social and behavioral factors affecting acquisition of infection, such as economic power imbalances between the sexes.
- Continue to characterize behavioral risk factors for transmission in specific populations and geographic areas.
- Continue to characterize the natural history of HIV infection in diverse geographic settings.
- Examine the role of co-infection with other endemic diseases in modulating HIV, including risk of acquiring and/or transmitting infection and disease progression.
- Define the spectrum, incidence, and risk factors for HIV-associated complications of HIV-related illness (e.g., OIs, malignancies, and neurological conditions) specific to individual regions prevalent in diverse geographic settings.
- Study the impact of prevention and treatment of HIV-related infections on HIV disease progression and transmission.
- Identify conditions that emerge as a consequence of ART and longer survival, such as malignancies, neurological and neuropsychological conditions, and metabolic and nutritional dysfunction.
- Conduct comparative epidemiological studies of substance use and HIV risk in settings of varying cultural conditions and HIV seroprevalence.

- Evaluate the risk of transmission through intravenous drug use with respect to the availability of sterile needles and syringes.
- Investigate the impact of alcohol and other drug abuse/dependence on HIV disease progression, adherence to treatment regimens, and clinical outcomes.
- Improve the quality of culturally appropriate self-reports of sexual risk behaviors.
- Develop biomarkers that can serve as surrogates for measurement of HIV risk behavior and can be used to predict and monitor rapid escalation of HIV epidemics.

APPENDIX A:

NIH Institutes and Centers

NIH INSTITUTES AND CENTERS

NCI	National Cancer Institute
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NHGRI	National Human Genome Research Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD	National Institute of Child Health and Human Development
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NINDS	National Institute of Neurological Disorders and Stroke
NIDA	National Institute on Drug Abuse
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIMH	National Institute of Mental Health
NINR	National Institute of Nursing Research
NLM	National Library of Medicine
CC	Warren Grant Magnuson Clinical Center
CIT	Center for Information Technology
NCCAM	National Center for Complementary and Alternative Medicine
NCRR	National Center for Research Resources
FIC	Fogarty International Center
CSR	Center for Scientific Review
NCMHD	National Center on Minority Health and Health Disparities
NIBIB	National Institute of Biomedical Imaging and Bioengineering

APPENDIX B:

FY 2003 OAR Planning Group for International Research

FY 2003 INTERNATIONAL RESEARCH PLANNING GROUP

Non-NIH Participants

Sten Vermund, M.D., Ph.D., Co-Chair
Professor
John J. Sparkman Center for International Public Health Education
Director
Division of Geographic Medicine
University of Alabama at Birmingham

Susan Allen, M.D., M.P.H.
Associate Professor of Epidemiology
University of Alabama at Birmingham School of Public Health

David D. Celentano, Sc.D., M.H.S.
Professor
Infectious Diseases Program
Department of Epidemiology
Johns Hopkins University School of Hygiene and Public Health

Myron S. Cohen, M.D.
Director
Department of Infectious Diseases
University of North Carolina at Chapel Hill

Josephine H. Cox, Ph.D.
Principal Investigator
U.S. Military HIV Research Program

Carlos del Rio, M.D.
Associate Professor
Department of Medicine
Division of Infectious Diseases
Emory University School of Medicine

Paul Delay, M.D.
Chief
HIV/AIDS Division
Global Bureau
U.S. Agency for International Development

Don C. Des Jarlais, Ph.D.
Director of Research
Chemical Dependency Institute
Beth Israel Medical Center

Wafaie Fawzi, M.D., Dr.PH.
Assistant Professor
International Nutrition and Epidemiology
Harvard University School of Public Health

Brooks Jackson, M.D.
Professor of Pathology
Department of Pathology
Johns Hopkins University

Warren Johnson, M.D.
Professor
Division of International Medicine
Department of Medicine
Cornell University Medical College

Claudes Kamenga, M.D., M.P.H.
Associate Director, CARE
Family Health International

Chirasak Khamboonruang M.D., Ph.D.
Research Institute for Health Sciences
Chiang Mai University

Wayne C. Koff, Ph.D.
Vice President
Research and Development
International AIDS Vaccine Initiative

Michael H. Merson, M.D.
Dean of Public Health
Department of Epidemiology and Public Health
Yale University School of Medicine

Nancy S. Padian, Ph.D., M.P.H., M.S.
Professor
Department of Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco

Philip O. Renzullo, Ph.D., M.P.H.
Epidemiologist
U.S. Military HIV Research Program

Zeda F. Rosenberg, Sc.D.
Scientific Director
HIV Prevention Trials Network
Family Health International

Jaime Sepulveda-Amor, M.D.
Instituto Nacionalde Salud Publica, Mexico

Swarup Sarkar, M.B.B.S., M.D.
Intercounty Programme Adviser
Joint United Nations Programme on HIV/AIDS

Mauro Schechter, M.D., Ph.D.
Professor of Infectious Diseases
Head
AIDS Research Laboratory
Hospital Universitario Clementino Fraga Filho

David Stanton, M.P.H.
Senior Technical Advisor
HIV/AIDS Division
Global Bureau
U.S. Agency for International Development

J. Roberto Trujillo, M.D., Sc.D.
President
Pan-American Society of Neurovirology
Harvard University School of Public Health

Stefan Z. Wiktor, M.D.
Associate Director
Global AIDS Program
Centers for Disease Control and Prevention

Zunyou Wu, M.D., Ph.D.
Director
Department of Behavioral Intervention
National Center for AIDS Prevention and Control

NIH Participants

Ms. Linda J. Reck, Co-Chair
Senior Policy Analyst
Program Planning and Evaluation
Office of AIDS Research, NIH

Jodi Black, Ph.D.
Program Director
National Cancer Institute, NIH

Helen Cesari, M.Sc.
Associate Director for Research Management
Center on AIDS and Other Medical Consequences of Drug Abuse
National Institute on Drug Abuse, NIH

Henry L. Francis, M.D.
Director
Center on AIDS and Other Medical Consequences of Drug Abuse
National Institute on Drug Abuse, NIH

F. Gray Handley, M.S.P.H.
Associate Director
Prevention Research and International Programs
National Institute of Child Health and Human Development, NIH

Rodney Hoff, D.Sc., M.P.H.
Senior Epidemiologist for International Research
Division of AIDS
National Institute of Allergy and Infectious Diseases, NIH

Dionne J. Jones, Ph.D.
Health Scientist Administrator
Center on AIDS and Other Medical Consequences of Drug Abuse
National Institute on Drug Abuse, NIH

Jonathan M. Kagan, Ph.D.
Acting Associate Director
Division of AIDS
National Institute of Allergy and Infectious Diseases, NIH

Barbara E. Laughon, Ph.D.
Chief
Opportunistic Infections Research Branch
Division of AIDS
National Institute of Allergy and Infectious Diseases, NIH

Donna Mayo, Ph.D.
Assistant Director for International Affairs
National Institute of Mental Health, NIH

Jeanne McDermott, Ph.D., CNM, M.P.H.
Program Officer
Division of International Training and Research
Fogarty International Center, NIH

Paolo G. Miotti, M.D., M.P.H.
Chief
Epidemiology Branch
Basic Science Program
Division of AIDS
National Institute of Allergy and Infectious Diseases, NIH

Susan Newcomer, Ph.D.
Statistician
Demographic and Behavioral Sciences Branch
Center for Population Research
National Institute of Child Health and Human Development, NIH

Willo Pequegnat, Ph.D.
Associate Director for Prevention and Translation Research
Division of Mental Disorders, Behavioral Research and AIDS
National Institute of Mental Health, NIH

Ms. Wendy Wertheimer
Senior Advisor
Office of AIDS Research, NIH

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

Anne Willoughby, M.D., M.P.H.
Acting Director
Center for Research for Mothers and Children
Branch Chief
Pediatric, Adolescent and Maternal AIDS Branch
National Institute of Child Health and Human Development, NIH

APPENDIX C:

List of Acronyms

LIST OF ACRONYMS

ART	antiretroviral therapy
ACTIS	AIDS Clinical Trials Information Service
AIDS	acquired immunodeficiency syndrome
AITRP	AIDS International Training and Research Program, FIC
ATI	Analytic Treatment Interruption
ATIS	HIV/AIDS Treatment Information Service
AVEG/HVTN	AIDS Vaccine Evaluation Group/HIV Vaccine Trials Network
BSL	biosafety level
B/START	Behavioral Science Track Award for Rapid Transition
CAB	community advisory board
CBO	community-based organizations
CDC	Centers for Disease Control and Prevention
CFAR	Centers for AIDS Research
CIPRA	Comprehensive International Programs in Research on AIDS
CMV	cytomegalovirus
CNS	central nervous system
CSF	cerebrospinal fluid
CTL	cytotoxic T lymphocytes
DC	dendritic cell
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
DOT	directly observed therapy
EBV	Epstein-Barr virus
FDA	Food and Drug Administration
FIRCA	Fogarty International Research Collaboration Award, FIC
GCP	Good Clinical Practices
GCRC	General Clinical Research Center
GI	gastrointestinal

GLP/GMP	good laboratory practices/good manufacturing production
HAART	highly active antiretroviral therapy
HBCU	Historically Black Colleges and Unviersities
HBV	hepatitis B virus
HCFA	Health Care Financing Administration
HCV	hepatitis C virus
HERS	HIV Epidemiology Research Study
HHV	human herpes virus
HIV	human immunodeficiency virus
HPTN	HIV Prevention Trial Network
HPV	human papillomavirus
HRSA	Health Resources and Services Administration
HVTN	HIV Vaccine Trials Network
IC	Institute and Center
ICC	invasive cervical cancer
IDU	injecting drug user
IHS	Indian Health Service
IUD	intrauterine device
JCV	JC virus
KS	Kaposi's sarcoma
KSHV	Kaposi's sarcoma herpes virus
LRP	Loan Repayment Program, NIH
MAC	*Mycobacterium avium* complex
MCT	mother-to-child transmission
MDR-TB	multiple drug-resistant tuberculosis
MHC	major histocompatibility complex
MSM	men who have sex with men
N9	nonoxynol
NAFEO	National Association for Equal Opportunity in Higher Education
NGO	nongovernment organizations

NHL	non-Hodgkin's lymphoma
NHP	non-human primate
NIH	National Institutes of Health
NRTIs	nucleoside reverse transcriptase inhibitors
OAR	Office of AIDS Research, NIH
OARAC	Office of AIDS Research Advisory Council
OD	Office of the Director, NIH
OI	opportunistic infection
PHS	Public Health Service
PML	progressive multifocal leukoencephalopathy
RCMI	Research Center in Minority Institution
RCT	randomized clinical trials
RFIP	Research Facilities Infrastructure Program
RNA	ribonucleic acid
RPRC	Regional Primate Research Center
SAMHSA	Substance Abuse and Mental Health Services Administration
SCID	severe combined immunodeficiency
SHIV	chimeric simian/human immunodeficiency virus
SIT	scheduled intermittent therapy
SIV	simian immunodeficiency virus
SPF	specific pathogen-free
STD	sexually transmitted disease
STI	Structured Treatment Interruption
TB	tuberculosis
TI	treatment interruption
UNAIDS	United Nations Joint Programme on AIDS
VEE	Venezuelan equine encephalitis virus
VRC	Vaccine Research Center
WHO	World Health Organization
WIHS	Women's Interagency HIV Study

Office of AIDS Research, National Institutes of Health
Building 2, Room 4W01 (MSC 0255)
Two Center Drive, Bethesda, Maryland 20892
Tel: 301-402-8655, Fax: 301-402-8638

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