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Appendices - Walk Through Edits & White House Graphics 8/27/96 [1]

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Appendix A

Current Federal Activities

PREVENTION

Agency: **Department of Defense**

Goal: To preserve of an effective fighting force through prevention of HIV infection.

Objective 1:

Prevent HIV infection in service members.

Reduce the number of new active duty HIV infection by 20 percent by 1997 based on a 1995 baseline figure of 204 persons for all services.

Action Steps: Provide basic information on HIV transmission and risk reduction for new recruits, civilian work force members, and officers.

Require education and general military training on methods of transmission and approaches for avoiding transmission, including barrier methods, avoidance of intravenous drug use, and use of universal precautions.

Provide training for personnel, instructors, and peer educators

Support train the trainer courses to develop multidisciplinary teams from medical, dental, nursing, and public health corps for promoting HIV and AIDS education.

Objective 2:

Ensure safety of the Armed Services Blood Program Office (ASBPO).

Action Steps: Advise service personnel with serologic evidence of HIV infection or repeated ELISA reactivity, but Western Blot negative or indeterminate, to refrain from donating blood.

Employ ASBPO "Look Back Program" to trace contacts of identified positive donors who serconvert after blood donation — trace and contact blood recipients.

Resources:

FY 95: Approximately ~~$11,660,000~~ 11.7 million

FY 96: Approximately ~~$12,000,000~~ 12.0 million

FY 97: Approximately ~~$12,380,000~~ 12.9 million

Populations Served: Active duty service members and their eligible family members, health care providers and those at risk of exposure to body fluids, and recipients of ASBPO blood products.

Constituency Involvement: Active duty force, affiliated civilian workforce, and the health care and public health communities.

Agency: **Department of Education**

Goal: To disseminate information on Department of Education Programs in coordination with other Federal agencies.

Objective 1:

Coordinate with DHHS to provide information and points of contact for existing Department of Education programs.

Action Steps: Coordinate and share information with CDC-sponsored National AIDS Clearinghouse; include information related to school-based comprehensive health programs (ED funded) in the Comprehensive Health Information Database (HHS).

Descriptions: A broad range of programs are supported; for example, including the Foundation For Children With AIDS, Duke University Medical Center, and University of California Disability Statistics Rehabilitation Research and Training Center.

Resources:

FY 95: Funding for AIDS prevention initiatives is part of the overall grant budget through the comprehensive school health program.

FY 96: Funding for AIDS prevention initiatives is part of the overall grant budget through the comprehensive school health program.

FY 97: Funding for AIDS prevention initiatives is part of the overall grant budget through the comprehensive school health program.

Populations Served: Elementary and secondary students, teachers and parents through health education curricular, pre-service, and in-service training and parental involvement programs.

Constituency Involvement: The majority of ED programs are developed at the local level and therefore there is little involvement of constituency groups at the Federal level.

Objective 2:

Identify informational needs of schools regarding HIV/AIDS and disseminate information that addresses those needs.

Action Steps: Using existing survey data, identify informational gaps.

Coordinate with the CDC on the School Health Information Planning Program (SHIPP).

Identify public and private agencies and groups that have developed HIV-related materials appropriate for school-based programs.

Catalog and distribute information on these resources.

Establish process to inform schools about resources available to address HIV/AIDS education and prevention.

Provide schools with information on Federal resources.

Prepare publication on the relationship between HIV/AIDS to drug use.

Meet with the National Coordinating Committee and the Interagency Committee on School Health to assist in identifying areas of need and publicizing the availability of resources.

Descriptions: AIDS prevention information dissemination to schools in the context of high risk behaviors arising out of drug and alcohol use.

Resources:

FY 95: Funding for initiatives part of overall program plan for Safe and Drug-Free Schools National Programs.

FY 96: Funding for initiatives part of overall program plan for Safe and Drug-Free Schools National Programs.

FY 97: Funding for initiatives part of overall program plan for Safe and Drug-Free Schools National Programs.

Populations Served: Elementary and secondary students, teachers and parents through health education curricular, pre-service, and in-service training and parental involvement programs.

Constituency Involvement: The majority of ED programs are developed at the local level and therefore there is little involvement of constituency groups at the Federal level.

Agency: Department of Health and Human Services, Agency for Health Care Policy and Research

Goal: To provide national estimates of the cost and use of HIV-related prevention services.

Objective 1:

To examine the effects of an in-home computer information and support system on health care costs and quality of life.

Action Steps: Half of three hundred patients with advanced HIV infection are provided with in-home computer system; the other half receive no intervention. Effects of this system are assessed with respect use of prophylactic treatments, early detection of infections, and quality of life.

Descriptions: Demonstrating Computer Support Impact on AIDS Patients.

Resources:

FY 95: $704,655

FY 96: $56,453

FY 97: $0

Populations Served: 300 volunteers with advanced HIV infection.

Constituency Involvement: Persons with HIV.

Objective 2:

Evaluate the cost-effectiveness of alternative strategies for preventing HIV-related opportunistic infections.

Action Steps: Embed clinical and cost data from randomized trials and observational cohorts into a comprehensive decision-analytic, cost-effectiveness model.

Descriptions: Cost-Effectiveness of Preventing AIDS Complications.

Resources:

FY 95: $346,420

FY 96: $21,020

FY 97: $0

Populations Served: Persons with HIV.

Constituency Involvement: NA.

Agency: **Department of Health and Human Services, Centers for Disease Control and Prevention~~develop new surveillance systems.~~**

Goal 1: To more accurately monitor the HIV epidemic and provide data to assess and direct prevention programs by strengthening existing systems and develop new surveillance systems.

Objectives:

Implement projects that evaluate and expand the uses of HIV infection and AIDS case surveillance and sero-surveillance data so that these data systems can more effectively guide public health policy and provide relevant information necessary to direct and evaluate prevention activities.

Improve understanding of the natural history of HIV infection as well as the risk factors and protective factors for sexual, drug-related, perinatal, and healthcare worker related HIV transmission in order to develop more effective prevention strategies for all affected populations.

Action Steps: Evaluate HIV infection reporting systems (named, anonymous, unique identifier) used nationally for their ability to monitor the epidemic, provide linkages to medical and social services, and to assess their impact on a person's decision to be tested.

Characterize high-risk behaviors of persons with evidence of recent HIV infection such as persons with documented HIV seroconversion, high CD4+ counts, or diagnosis of HIV infection in adolescents.

Assess the impact of public health guidelines and recommendations and prevention efforts.

Characterize persons co-infected with TB and HIV.

Evaluate ways to improve the completeness and quality of risk ascertainment on persons reported with HIV and AIDS.

Centers for Disease Control and Prevention, continued

Identify and characterize previously unreported AIDS cases among deaths investigated by local medical examiners to assess the impact of under-diagnosis of AIDS cases on AIDS surveillance among disadvantaged populations that often do not receive adequate health care.

Test the efficiency of new techniques for reporting HIV and AIDS surveillance data from health care providers and laboratories to health departments.

Collect additional data on persons reported through HIV/AIDS surveillance which may be important for the planning and evaluation of prevention and care programs, such as social/economic status, levels of disabilities, drug use history, sex behavior history, utilization of HIV testing and medical care services, and reproductive history in women.

Assess the interrelationship of behaviors, HIV markers and surrogates, and their potential role in surveillance systems.

Assess the interaction of socioeconomic, behavioral, and biologic factors in HIV transmission.

Determine the role of female-specific biological factors that are linked to acquisition and transmission of HIV infection and that influence the course of HIV disease.

Determine factors contributing to the efficiency of sexual transmission of HIV.

Assess the risk of transmission of HIV and TB from HIV-infected health-care worker to patient and vice versa.

Develop systems to monitor the emergence of multidrug-resistant TB in the HIV infected.

Continue to develop improved methods for projecting or modeling the HIV epidemic.

Develop methods to differentiate HIV-specific antibodies generated in participants in HIV vaccine trials from those generated in response to HIV infection.

Develop methods to identify potential cases of HCW-to-patient transmission.

Expand HIV reporting systems to collect information about primary and secondary HIV prevention services needed and received by HIV-positive clients (in collaboration with HRSA).

Work with providers and users of lab services to develop & implement systems which provide assurance that the capacity and quality requirements for HIV testing are met.

Work with international partners to study TB, implement vaccine trials, enhance clinical management, assess prevention efficacy, and improve program management of HIV/AIDS.

Develop methods to evaluate the use of HIV infection and AIDS surveillance systems to assess early intervention strategies.

Descriptions: Many of the activities in the above-cited action steps are carried out through cooperative agreements with state and local health departments. In addition, specialized projects and studies also serve to focus attention on these activities, these include: Evaluation of HIV Infection Reporting Systems Project, Recent HIV Infection Projects, Surveillance to Evaluate Prevention Projects, Adult Spectrum of Disease Project, the TB Project, Mode of Transmission Validation Project, the Medical Examiner Study, and the Enhancement of AIDS Surveillance Efficiency Project.

Resources:

FY 95: ~~$141,046,000~~ 141 million
FY 96: ~~$139,668,000~~ 140 million
FY 97: ~~$139,778,000~~ 140 million

Centers for Disease Control and Prevention, continued

Populations Served: All major racial, ethnic, and risk groups.

Constituency Involvement: There is regular consultation with national, State, and local public health officials and many other relevant organizations such as HIV-related community-based organizations.

Goal 2: To increase the public understanding of, involvement in, and support for HIV prevention.

Objectives:

Provide leadership in HIV and STD prevention by (1) establishing sustained and active national agenda through the media; (2) promoting credible messages based on science through credible channels; and (3) encouraging and supporting prevention efforts at the local level.

Establish a collaboration of partners composed of national, State, and local organizations to facilitate (1) diffusing social marketing principles applied to HIV and STD prevention at the local level; (2) identifying and promoting mechanisms to exchange technology and information; and (3) developing guidelines for applying social marketing principles to local HIV and STD prevention.

Apply social marketing principles at the local level for the purpose of (1) demonstrating the participatory social marketing process (i.e., skills and resources needed to effectively engage the community); (2) measuring the effects of behavior-based social marketing interventions; and, (3) documenting the lessons learned.

Facilitate the application of prevention marketing principles in CDC-funded community planning efforts by (1) promoting guidelines for consideration of these principles at the local level for prevention interventions and (2) providing interactive technical assistance on social marketing technology principles (or prevention marketing) to public health agencies as well as HIV Prevention Community Planning Groups.

Promote HIV prevention as a relevant issue in business settings.

Provide and promote a network of resources and referrals to assist in implementing the Business Responds to AIDS (BRTA) Comprehensive HIV/AIDS Workplace Program.

Market the comprehensive workplace HIV/AIDS program to business.

Establish and execute a research agenda to formulate and assess strategies and resources to advance the knowledge of effective workplace HIV programs.

Develop performance measures to assess effectiveness of CDC prevention efforts.

Action Steps: Monitor changes in public knowledge about how HIV is and is not transmitted.

Develop methodologies to measure community mobilization or changes in institutional behavior in relation to mass media public information and education programs.

Develop new mass media messages, in collaboration with the public health systems and with international, national, state, and local private sector organizations and agencies.

Centers for Disease Control and Prevention, continued

Expand the relationship between CDC and the entertainment industry to improve messages and role modeling for HIV prevention;

Develop communication interventions with appropriate organizations to ensure that consistent, accurate HIV prevention information is provided to the public.

Develop community coalitions for HIV prevention.

Coordinate and disseminate information messages through the media that explain new scientific findings and policies concurrent with the release of new scientific information.

Develop leadership of health/education officials to effectively deliver HIV prevention messages through partnerships.

Evaluate the role of communications in changing individual knowledge, community norms, and individual behavior through establishment of model programs.

Expand the relationship between CDC and academic experts in mass communications to develop methods for measuring the impact of mass media on individual and community behaviors.

Develop ways of measuring the mobilization of community groups, i.e., changes in community norms, capacity.

Monitor business policies and employee education programs regarding HIV/AIDS;

Implement a BRTA initiative to develop HIV prevention and service programs for the work-place and the community.

Sponsor and participate in national meetings of businesses and religious, civic, medical, social, and voluntary agencies which conduct HIV prevention and service programs.

Descriptions: Many of the activities cited above are carried out at local demonstration sites and in coordination with community planning efforts. In addition, specialized projects and studies also serve to focus attention on these activities, these include projects entitled: National Health Communications, Prevention Collaborative Partners, the CDC National AIDS Clearinghouse, and the CDC National AIDS Hotline, and the Prevention Marketing Initiative.

Also, linkage efforts with business, labor, and community groups have received special attention. The Business Responds to AIDS (BRTA) and Labor Responds to AIDS (LRTA) programs have focused on issues such as: HIV/AIDS workplace policies, supervisor and labor leader training, employee education, employee family education, and community service and volunteerism. Partnerships have also been forged among a variety of communities including business, labor, religious, voluntary and the media. And, national and regional minority organizations have also been sought out in forging these important linkages.

Resources:

FY 95: ~~$45,960,000~~[e] 46 million

FY 96: ~~$45,512,000~~[e] 45 million

FY 97: ~~$45,547,000~~[e] 46 million

Populations Served: All segments of the population including all major racial and ethnic groups, young persons (18-25), persons engaging in behaviors that place them at risk for HIV infection, and business and labor leaders including their employees and families.

Centers for Disease Control and Prevention, continued

Constituency Involvement: Regular consultation with leaders from over 200 prevention collaborative partners composed of national, state, and local organizations and over 50 business and labor partners.

Goal 3: To prevent risk behaviors that can cause HIV infection and related health problems in school age children and college age youth through implementation of comprehensive school health education programs.

Objectives:

Increase by 15 percent the proportion of school districts that require age-appropriate HIV education at each grade level, K-12, especially at grades 9-12, preferably as part of comprehensive school health education.

Increase by 15 percent the proportion of colleges and universities that provide HIV education for students and staff, preferably as part of an institution-wide health promotion program.

Decrease by 10 percent at each grade level the proportion of 9th to 12th grade students who report they have engaged in sexual intercourse.

Among 9th to 12th grade students who report they have engaged in sexual intercourse, decrease by 10 percent the proportion who report they have engaged in sexual intercourse during the past 3 months.

Among 9th to 12th grade students who report they have engaged in sexual intercourse during the past 3 months, increase by 10 percent the proportion who report they used a condom at last intercourse.

Decrease by 10 percent the proportion of 9th to 12th grade students who report they have injected illicit drugs.

Action Steps: Monitor state-level policy and program requirements that support effective HIV education within comprehensive school health education (CSHEs).

Monitor progress toward objectives.

Monitor district-level policy and program requirements that support effective HIV education within comprehensive school health education programs.

Monitor the prevalence of behaviors that cause HIV infection and related health problems among school and college youth.

Implement and revise as necessary, CDC guidelines for effective school health education to prevent the spread of HIV infection.

Enhance the capacity of State and local educational agencies to develop and implement effective HIV education within CSHEs.

Enhance the capacity of colleges and universities to provide HIV education for students and staff, preferably as part of an institution-wide health promotion program.

Centers for Disease Control and Prevention, continued

Ensure the integration of education to prevent HIV infection, other STDs and the use of alcohol and other drugs among youth.

Strengthen the capabilities of state and local departments of education and health to collaboratively help schools, colleges and universities implement effective HIV education programs for youth.

Increase the effectiveness of HIV education for youth served by State and local departments of education and colleges and universities through the efforts of selected national organizations.

Enhance the capacity of State and local agencies to help prevent HIV infection and HIV-related problems among youth through the efforts of training and demonstration centers established for State and local departments of education.

Establish teacher training coordinators in every interested State to help teachers provide effective HIV education within a CSHE.

Identify and disseminate, through training and demonstration centers and through teacher training directors, HIV education programs that have been shown to the be effective in reducing behaviors that cause HIV infection and related health problems.

Synthesize and apply the results of research to increase the effectiveness of HIV prevention education for youth.

Conduct formative evaluations of state and local departments of education policies, curricula, teacher training, and school efforts to prevent behaviors that cause HIV infection and related health problems.

Develop a standardized report for each State to profile the nature of priority health problems and risk behaviors among youth in that State and school efforts to prevent these problems and behaviors.

Conduct evaluations of the effectiveness of existing school-based interventions to reduce behaviors that result in HIV infection and related health problems.

Develop state-of-the-art school-based interventions and evaluate their effectiveness in reducing behaviors that result in HIV and related health problems.

Conduct and apply meta-evaluations of existing research data about the effectiveness of school-based interventions in reducing health risks behaviors among adolescents.

Descriptions: Funding and technical assistance for State and local educational agencies is provided through several avenues including national non-governmental organizations, colleges and universities, and teacher training sites. There is also support for youth surveys and projects to reach out-of-school youth.

Resources:

FY 95: ~~$48,205,000~~ 48 million
FY 96: ~~$47,735,000~~ 48 million
FY 97: ~~$47,771,000~~ 48 million

Populations Served: Young persons engaging in behaviors that place them at risk for acquiring HIV through sexual exposure, including all major racial and ethnic groups. All school- and college-aged youth regardless of school enrollment status.

Centers for Disease Control and Prevention, continued

Constituency Involvement: Consultation with a wide range of constituency groups was established to: (1) improve existing programmatic efforts; (2) improve assistance and resources provided by CDC; and, (3) explore strategies that the Nation might take to improve the health status of young people. These groups include representatives from: (1) every State education agency, District of Columbia, and six territorial education agencies; (2) national non-governmental health or education organizations, 3) colleges and universities, 4) State public health departments, as well as young people themselves. Meetings included an annual constituency meeting, quarterly training programs, and communication through an electronic bulletin board and network.

Goal 4: To prevent or reduce behaviors or practices which place individuals at risk of HIV infection, and for HIV positive individuals, place others at risk.

Objectives:

At least 90 percent of individuals with known HIV infection will be abstinent or will have used a condom at last sexual intercourse, and at least 50 percent of individuals who have engaged in high-risk sexual behaviors within the past 12 months will be abstinent, in a mutually monogamous relationship, or have used a condom at last sexual intercourse.

At least 75 percent of injecting drug users will have stopped injecting drugs or used sterile or decontaminated injection equipment at last injection.

At least 80 percent of the health care and public safety workplaces will implement programs and procedures for preventing HIV transmission at work sites.

Reduce unintended pregnancies to no more than 40 percent of pregnancies among women with or at risk for HIV infection.

The number of individuals donating blood and found to be infected with HIV at the time of donation will decrease by 50 percent through self-deferral.

Among selected populations of youth in high-risk situations, increase by 10 percent the proportion who report they used a condom at last sexual intercourse.

Action Steps: Collaborate with prevention partners to assess risk behaviors and practices in selected communities.

Monitor progress toward objectives.

Identify barriers to implementation of HIV prevention programs at community, state, and national levels.

Collaborate with selected communities in developing and implementing a model behavioral intervention program that comprehensively addresses community needs and uses available community resources and prevention partners in selected sites.

Design, develop, and test effective community-level interventions to change risk behaviors through altering community norms and values to support healthy behaviors.

Expand the community's capacity to plan, implement, and evaluate culturally competent and linguistically specific HIV prevention guidelines and programs tailored to the needs of specific populations.

Centers for Disease Control and Prevention, continued

Enhance the capacity of CDC staff to plan, administer, and evaluate behavioral change strategies and community-based interventions to provide public health leadership and assist our prevention partners in designing and managing effective strategies for HIV prevention programs.

Enhance the capacity of local health departments and other relevant community agencies to collaboratively provide effective HIV education for youth in high-risk situations.

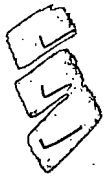
Establish scientifically-based evaluation components for HIV prevention activities.

Use evaluation of components to design or refine HIV prevention programs and/or redirect HIV prevention resources.

Descriptions: Several mechanisms are employed for achieving the goals and objectives cited above. These include cooperative agreements with State and local health departments, in addition to direct funding of community-based organizations, national organizations, and national minority organizations. HIV intervention research studies are also supported.

Resources:

FY 95: ~~$185,625,000~~ 186 million
FY 96: ~~$183,814,000~~ 184 million
FY 97: ~~$203,958,000~~ 204 million



Populations Served: All major racial and ethnic groups in addition to persons engaging in behaviors that place them at risk for acquiring HIV.

Constituency Involvement: A major avenue for constituency involvement is the HIV Prevention Community Planning Process. Through this mechanism, State and local health departments form community planning groups to assist in developing HIV prevention plans. In addition, there is regular and extensive consultation with representatives from state and local health departments, community planning groups, and national organizations.

Goal 5: To increase individual knowledge of serostatus and strengthen systems for successful referral to early intervention services.

Objectives:

At least 85 percent of the estimated 800,000 to 1,000,000 HIV-infected individuals will know their HIV serostatus.

At least 90 percent of health care sites receiving public funds and serving at-risk persons will provide appropriate HIV counseling and testing services.

At least 80 percent of known HIV infected individuals, either directly or through referral, will receive primary and secondary prevention services.

Action Steps: Working with governmental and nongovernmental partners, enhance community-level assessments of needed primary and secondary prevention services.

Centers for Disease Control and Prevention, continued

Monitor progress toward objectives.

Identify opportunities for common HIV prevention data collection and development of uniform data sets.

Integrate HIV prevention services into standards of care for the diagnosis and treatment of HIV disease.

In collaboration with the FDA, develop, test, and implement rapid HIV testing procedures.

Strengthen the capacity of State, and local health departments to provide partner notification services to private health care providers offering HIV counseling and testing.

Develop alternative methods to provide HIV counseling and testing services.

Work with professional groups, hospitals, and State health departments to ensure that health care workers receive adequate training on primary and secondary HIV prevention (in collaboration with HRSA).

Study the impact of discrimination as a barrier to prevention services.

Assist publicly funded counseling and testing sites establish selection criteria and systems for monitoring the quality of referral laboratories.

Interview persons newly diagnosed with HIV infection to identify missed opportunities for earlier diagnosis and CD4+ testing.

Conduct a study of incident AIDS cases to determine what services HIV-positive clients are receiving over time to identify service gaps (in collaboration with HRSA).

Provide guidelines and training to HIV counselors to improve the quality of counseling.

Descriptions: Counseling, testing, referral partner notification programs are supported as part of cooperative agreements with state and local health departments.

Resources:

FY 95: ~~$168,995,000~~ 169 million
FY 96: ~~$167,351,000~~ 167 million
FY 97: ~~$181,027,000~~ 181 million

Populations Served: All major racial and ethnic groups and persons engaging in behaviors that place them at risk for acquiring HIV.

Constituency Involvement: A major avenue for constituency involvement is the HIV Prevention Community Planning Process. Through this mechanism, State and local health departments form community planning groups to assist in developing HIV prevention plans. In addition, there is regular and extensive consultation with representatives from State and local health departments, community planning groups, and national organizations.

~~Centers for Disease Control and Prevention, continued~~

Agency: Department of Health and Human Services, Food and Drug Administration

Goal: To reduce transfusion-transmitted HIV infection.

Objective:

Ensure supply and safety of the national blood supply.

Action Steps: Establish policies, expedite review of product applications, conduct approval inspections, oversee surveillance, and support enforcement activities.

Descriptions: Encourage high risk donors to exclude themselves; update list of unsuitable donors; quarantine and test blood; investigate incidents to identify, and rectify common errors in blood banks.

Resources:

FY 95: ~~$17,458,000~~ 17.5 million
FY 96: ~~$17,458,000~~ 17.5 million
FY 97: ~~$17,458,000~~ 17.5 million

Populations Served: All persons who may receive blood or blood products.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Agency: Department of Health and Human Services, Health Care Financing Administration

Goal: To reduce perinatal transmission among Medicaid-eligible women.

Objectives:

Develop and implement a campaign to inform HIV positive women in selected pilot areas about the benefits of AZT in FY 95.

Expand pilot project to one State in all regions in FY 96.

Expand project to include all States in FY 97.

Action Steps: Develop, obtain, and distribute brochures and other materials describing current guidelines for the use of AZT during pregnancy for preventing perinatal transmission, and Medicaid eligibility and coverage to Medicaid eligible women.

Descriptions: Establish a consumer-oriented educational campaign in key States with high HIV prevalence rates among women.

Resources:

FY 95: $50,000 (Federal share)

FY 96: $60,000 (Federal share)

FY 97: $185,000 (Federal share, subject to availability of funds)

Populations Served: HIV-positive women eligible for Medicaid coverage.

Constituency Involvement: Significant consultation with high-risk pregnant women and their advocates.

Agency: **Department of Health and Human Services, Health Resources and Services Administration**

Goal: To reduce the perinatal transmission of HIV.

Objective:

Enhance provider capacity to provide appropriate services for women at the community level.

Improve provider capacity for outreach, counseling, testing and care for women of childbearing age for early identification and linkage to care for pregnant women.

Enhance providers' abilities to provide AZT for HIV positive pregnant women.

Ensure funding and dissemination of innovative models of care that evaluate all of the major care and service goals listed in this plan: effectively educated providers, increased access to and quality of care, reduction of perinatal transmission of HIV.

Action Steps: Establish the Women's Initiative for HIV Care for Women and Reduction of Perinatal Transmission (WIN).

Establish ongoing WIN Steering Committee.

Provide technical assistance to grantees.

Conduct centralized training for all WIN sites with follow-up local training.

Collaborate with Association of Maternal & Child Health Programs (AMCHP) to develop local guidelines.

Establish MCHB working group to coordinate HIV risk reduction related efforts across programs.

Distribute counseling and testing guidance, AHCPR consumer brochure and video, and other PHS documents to MCHB community.

Review currently funded SPNS projects to identify gaps in project coverage for future Requests for Applications (RFAs).

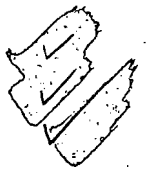
Evaluate sites.

Descriptions: Enhance outreach for HIV counseling and testing. Improve service linkages for women of childbearing age in an ongoing care system and to reduce perinatal HIV transmission. PHS 076 Implementation Plan.

Health Resources and Services Administration, continued

Resources:

FY 95: ~~$1,520,000~~ 1.5 million
FY 96: ~~$1,800,000~~ 1.8 million
FY 97: ~~$1,890,000~~ 1.9 million



Populations Served: CARE Act grantees. Adolescent and adult women and their infants, with special attention for pregnant women in addition to MCH and HIV providers.

Constituency Involvement: Health care providers, evaluation researchers, communication experts, and patient advocates. There is also consumer participation in WIN steering committee and projects advisory boards in addition to linkages with other HRSA grantees including those from RWCA and SPNS programs.

Agency: Department of Health and Human Services, Indian Health Service

Goal: To reduce the number of new infections among federally recognized American Indians and Alaska Natives.

Objective 1:

Maintain surveillance of HIV infection in American Indians and Alaska Natives.

Action Steps: Maintain timely and complete case reporting to appropriate local, state and national entities and the Indian Health Service (IHS) AIDS Prevention Activities Office.

Descriptions: Area AIDS Coordinators will be responsible for reporting.

Resources:

FY 95: $ ~~912,000~~ 3.6 million
FY 96: $ ~~912,000~~ 3.7 million
FY 97: ~~$1,800,000~~ 3.8 million

Populations Served: Federally recognized American Indians and Alaska Natives.

Constituency Involvement: Local and National Indian Health Advisory Boards.

Objective 2:

Maintain training and information activities to provide health education and risk reduction messages.

Action Steps: Teach empowerment skills at the individual and community level that will enhance the individual's ability to actualize assimilated knowledge as behavior change.

Descriptions: HIV health education and risk reduction message dissemination.

Resources:

FY 95: Part of overall IHS budget.

FY 96: Part of overall IHS budget.

FY 97: Part of overall IHS budget.

Populations Served: American Indians and Alaska Natives population, tribal leaders, women, youth, individuals practicing high risk behavior, and IHS/tribal health care workers.

Constituency Involvement: Local and National Indian Health Advisory Boards.

Agency: **Department of Health and Human Services, National Institutes of Health**

Goal: To conduct and support behavioral and social science research to further understanding of the determinants and processes that influence behaviors associated with HIV transmission and to develop and improve HIV prevention intervention strategies, and, to conduct and support natural history and epidemiological research to improve the understanding of the risk factors and mechanisms of HIV transmission and disease progression and to develop prevention strategies to reduce or prevent HIV transmission.

NIH's efforts in these areas can be found in Appendix B: Research.

Agency: **Department of Health and Human Services, Office of Population Affairs**

Goal: To reduce the number of new HIV infections.

Objective:

Provide counseling, education, and HIV testing as needed to Title X program clinics.

Action Steps: Include HIV/AIDS education in all clinic education programs.

Include HIV/AIDS prevention in STD screening programs.

Provide HIV testing or referral for testing to all Title X clients who request testing.

Descriptions: Title X Program.

Resources:

FY 95: NA — HIV services integrated into overall budget.

FY 96: NA — HIV services integrated into overall budget.

FY 97: NA — HIV services integrated into overall budget.

Populations Served: The Title X program provides family planning and related reproductive health services to approximately 4.5 million clients annually through a network of 4,500 clinics. Clients are predominantly young women; most are members of low-income families, and 30 percent are adolescents and 33 percent are below age 25.

Constituency Involvement: For non-profit grantees, clients participate on boards of directors. For all grantees, clients participate on committees approving all information and education materials.

Agency: **Department of Health and Human Services, Substance Abuse and Mental Health Services Administration**

Goal: To reduce the number of new HIV infections.

Objective:

Demonstrate the effectiveness of incorporating HIV/AIDS prevention curricula into ongoing substance abuse prevention programs.

Demonstrate the differential effectiveness of incorporating HIV/AIDS prevention curricula into ongoing substance prevention programs.

Action Steps: Supplementation of high risk youth grants for alcohol, tobacco and other drugs (ATOD) prevention for the purpose of including HIV/AIDS prevention strategies in their present activities.

Develop program to empower youth with skills, knowledge, and beliefs for HIV prevention.

Demonstrate effective strategies to prevent ATOD use and abuse among high risk youth.

Include developmentally and culturally appropriate HIV/AIDS education and prevention approaches.

Descriptions: High Risk Youth Program.

Resources:

FY 95: $292,000

FY 96: $0

FY 97: $0*

* In addition, SAMHSA's Knowledge Development Application (KDA) Program includes an AIDS initiative in FY 1997. This initiative includes various approaches, including how best to: educate service providers, address family issues, interrupt HIV transmission, and maximize client retention in substance abuse treatment. The FY 1997 estimate for HIV/AIDS in the President's Budget is $15,000,000.

Populations Served: High risk youth or youth at risk for ATOD, adolescent females, and youth at risk for AOD-related violent behavior.

Constituency Involvement: Families of youth, youth service workers, and the communities that support youth at risk for ATOD abuse.

Agency: Department of Housing and Urban Development

Goal: To reduce the number of new infections among residents of public and subsidized housing.

Objective:

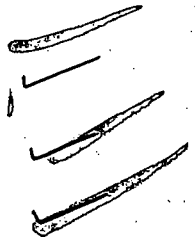
Provide primary prevention programs to public housing residents at risk for HIV infection. Coordinate meetings of the state and local agencies responsible for the prevention program services.

Action Steps: Forge local partnerships and improve coordination of existing resources.

Descriptions: HIV/AIDS Prevention in Public Housing Demonstration Program.

Resources:

FY 95: ~~$0~~ Activities carried out within existing HUD personnel resources.
FY 96: ~~$0~~ Activities carried out within existing HUD personnel resources.
FY 97: ~~$0~~ Activities carried out within existing HUD personnel resources.



Populations Served: Children and adults in public housing in five targeted cities.

Constituency Involvement: Input received through local planning groups.

Agency: Department of Justice

Goal 1: To reduce risk of infection of infection to INS detainees who are at risk.

Objective:

Educate detainees believed to be at risk regarding HIV/AIDS and thereby reduce the risk of transmission and new infections.

Action Steps: Upon obtaining informed consent, test detainees suspected of or diagnosed with HIV/AIDS or test upon detainee request and provide pre- and post-test counseling to detainees deemed at risk.

Descriptions: Provide limited testing and counseling.

Department of Justice, continued

Resources:

FY 95: Part of overall operating budget.

FY 96: Part of overall operating budget.

FY 97: Part of overall operating budget.

Populations Served: INS Detainees.

Constituent Involvement: None.

Goal 2: To reduce the risk of employee infection and avoid possible worksite performance problems.

Objective:

Educate Bureau of Prisons (BOP) staff, Drug Enforcement Agency (DEA) employees, Federal Bureau of Investigation (FBI) employees, Immigration and Naturalization Service (INS) employees, and U.S. Marshals Service (USMS) regarding HIV/AIDS transmission and thereby reduce the risk of infection. Educate all Justice Department employees about HIV/AIDS in the workplace.

Action Steps: For Bureau of Prison (BOP) staff provide: annual HIV information update and infectious disease training to all staff; produce inmate and staff HIV educational videos; and participate at least quarterly with HRSA in audio conferences on HIV issues.

For DOJ employees in occupations that possess a heightened possibility for exposure to HIV or other bloodborne pathogens, including employees of the DEA, FBI, INS, and USMS provide: general training and field office training; annual bloodborne pathogen training to all personnel as mandated by OSHA (discussion of HIV/AIDS is included in this training); and an annual update on the bloodborne pathogens training as necessary to discuss new information or changes in the use of safety equipment, etc.

For all Department employees, the Justice Management Division (JMD) provides: instructional materials to be used in a one time general training; and technical assistance to other DOJ components.

Descriptions: DOJ staff prevention training programs.

Resources:

FY 95: Part of overall operating budget.

FY 96: Part of overall operating budget.

FY 97: Part of overall operating budget.

Populations Served: DOJ employees.

Constituency Involvement: None.

Agency: **Department of Veterans Affairs**

Goal: To prevent transmission of HIV infection through education of employees and patients.

Objective 1:

Train and maintain cadre of professional staff to conduct HIV transmission and prevention education for patients and conduct pre- and post-test HIV antibody test counseling.

Action Steps: Establish national training program to educate two professional staff from every VA medical center to conduct patient education and pre- and post-test counseling.
Maintain on-going training program on limited basis to address turnover of staff and maintain cadre of counselors/patient educators.

Objective 2:

Educate and maintain cadre of knowledgeable staff to teach all staff in VA health-care facilities on prevention and transmission of HIV infection.

Action Steps: Develop a national "train the trainer" education program to educate selected staff from every VA Medical Center on how to organize and conduct staff educational activities on HIV transmission and prevention.

Update training materials/revise strategies to maintain knowledgeable base of trainers for every facility.

Objective 3:

Integrate HIV prevention education in addiction treatment programs.

Action Steps: Conduct national training program for professional staff in addiction treatment programs and Vet Centers on how to integrate HIV prevention education for patients in their treatment areas.

Objective 4:

Stimulate innovative approaches to HIV/AIDS education at the local level (VA Medical Centers and communities).

Action Steps: Award educational demonstration grants to HIV/AIDS education proposals on competitive basis.

Facilitate system-wide dissemination of completed projects through annual publication and national quarterly newsletters.

Department of Veterans Affairs, Continued

Objective 5:

Maintain education and information support systems.

Action Steps: Continue AIDS awareness and education programs through national system of regional education centers and individual facility programs.

Through library system, continue purchase of appropriate private and Federal sector videos, publications, posters, and other materials.

Objective 6:

Prevent transmission of HIV in the health-care setting.

Action Steps: Ensure on-going implementation of CDC recommendations on universal precautions, via policy.

Ensure continuing implementation of OSHA rule on protection of health-care workers against bloodborne pathogens via policy.

Provide national training program on interdisciplinary team training for staff from infection control, employee health, safety in all VAMCs to implement OSHA rule.

Descriptions: Prevention activities including education and universal precautions.

Resources:

FY 95: ~~$31,000,000~~* 31 million
FY 96: ~~$31,000,000~~* 31 million
FY 97: ~~$31,000,000~~* 31 million

* Figures are based on the estimated resource expenditures for universal precautions and education and are part of the general Medical Care Budget. FY 1996 and FY 1997 estimates are based on the resource levels contained in the President's budget.

Populations Served: Eligible veterans through local medical centers and facilities, local VA health-care and support staff, veteran patients and families, general public.

Constituency Involvement: VA medical centers and health-care facilities, and local communities.

Agency: Corporation for National Service

Goal: To offer HIV/AIDS education programs and other services with volunteers from the Learn and Serve America project.

Objective:

To promote HIV awareness through support HIV-related Learn and Serve America projects.

~~Department of Veterans Affairs~~, continued

Corporation for National Service

Action Steps: Continue programs for youth in elementary school or high school to volunteer in community service activities, such as peer education in HIV/AIDS prevention.

Continue to award grants to colleges and universities which provide service opportunities on HIV/AIDS prevention.

Program Description: Examples of higher education programs include Robert Wood Johnson Medical School and the University of San Diego where students provide HIV/AIDS education to homeless and other high risk populations.

Resources:

FY 95: Part of overall operating cost.

FY 96: Part of overall operating cost.

FY 97: Part of overall operating cost.

Populations Served: Persons living with HIV and AIDS and others who could benefit from HIV/AIDS education.

Constituency Involved: Both Learn and Serve America program participants and students across the country.

~~***Unmet Needs:*** Without these programs, students would not have an opportunity to serve their communities in HIV/AIDS-related projects.~~

Agency: Department of Defense

Goal: Preservation of an effective fighting force through prevention of HIV infection.

Objective 1: Prevent HIV infection in service members.

Reduce the number of new active duty HIV infection by 20 percent by 1997 based on a 1995 baseline figure of 204 persons for all services.

Action Steps: Provide basic information on HIV transmission and risk reduction for new recruits, civilian work force members, and officers;

Require education and general military training on methods of transmission and approaches for avoiding transmission, including barrier methods, avoidance of intravenous drug use, and use of universal precautions;

Provide training for personnel, instructors, and peer educators; and

Support train the trainer courses to develop multidisciplinary teams from medical, dental, nursing, and public health corps for promoting HIV and AIDS education.

Objective 2: Ensure safety of the Armed Services Blood Program Office (ASBPO).

Action Steps: Advise service personnel with serologic evidence of HIV infection or repeated ELISA reactivity, but Western Blot negative or indeterminate, to refrain from donating blood.

Employ ASBPO "Look Back Program" to trace contacts of identified positive donors who serconvert after blood donation -- trace and contact blood recipients.

FY 95: Approximately $500,000
FY 96: Approximately $500,000
FY 97: Approximately $500,000

Populations Served: Active duty service members and their eligible family members, health care providers and those at risk of exposure to body fluids, and recipients of ASBPO blood products.

Constituency Involvement: Active duty force, affiliated civilian workforce, and the health care and public health communities.

Unmet Need: None

Agency: Department of Education

Goal: To disseminate information on Department of Education (ED) Programs in coordination with other Federal agencies.

Objective 1: Coordinate with DHHS to provide information and points of contact for existing ED programs.

Action Steps: Coordinate and share information with CDC-sponsored National AIDS Clearinghouse; include information related to school-based comprehensive health programs (ED funded) in the Comprehensive Health Information Database (HHS).

Descriptions: A broad range of programs are supported; for example, including the Foundation For Children With AIDS, Duke University Medical Center, and University of California Disability Statistics Rehabilitation Research and Training Center.

FY 95: Funding for AIDS prevention initiatives is part of the overall grant budget through the comprehensive school health program.

FY 96: Funding for AIDS prevention initiatives is part of the overall grant budget through the comprehensive school health program.

FY 97: Funding for AIDS prevention initiatives is part of the overall grant budget through the comprehensive school health program.

Populations Served: Elementary and secondary students, teachers and parents through health education curricular, pre-service, and in-service training and parental involvement programs.

Constituency Involvement: The majority of ED programs are developed at local level and therefore there is little involvement of constituency groups at the Federal level.

Unmet Need: Many groups are unaware that resources are available to assist them. Increased funding would assist in improved information dissemination.

Objective 2: Identify informational needs of schools regarding HIV/AIDS and disseminate information that addresses those needs.

Action Steps: Using existing survey data, identify informational gaps.

Coordinate with the CDC on the School Health Information Planning Program (SHIPP).

Identify public and private agencies and groups that have developed HIV-related materials appropriate for school-based programs.

Catalog and distribute information on these resources.

Establish process to inform schools about resources available to address HIV/AIDS education and prevention.

Provide schools with information on Federal resources.

Prepare publication on the relationship between HIV/AIDS to drug use.

Meet with the National Coordinating Committee and the Interagency Committee on School Health to assist in identifying areas of need and publicizing the availability of resources.

Descriptions: AIDS prevention information dissemination to schools in the context of high risk behaviors arising out of drug and alcohol use.

FY 95: Funding for initiatives part of overall program plan for Safe and Drug-Free Schools National Programs.
FY 96: Funding for initiatives part of overall program plan for Safe and Drug-Free Schools National Programs.
FY 97: Funding for initiatives part of overall program plan for Safe and Drug-Free Schools National Programs.

Populations Served: Elementary and secondary students, teachers and parents through health education curricular, pre-service, and in-service training and parental involvement programs.

Constituency Involvement: The majority of ED programs are developed at local level and therefore there is little involvement of constituency groups at the Federal level.

Unmet Need: Many groups are unaware that resources are available to assist them. Increased funding would assist in improved information dissemination.

Agency: Department of Health and Human Services, Agency for Health Care Policy and Research

Goal: To provide national estimates of the cost and use of HIV-related prevention services.

Objective 1: To examine the effects of an in-home computer information and support system on health care costs and quality of life.

Action Steps: Half of three hundred patients with advanced HIV infection are provided with in-home computer system; the other half receive no intervention. Effects of this system are assessed with respect use of prophylactic treatments, early detection of infections, and quality of life.

Descriptions: Demonstrating Computer Support Impact on AIDS Patients

FY 95: $704,655
FY 96: $56,453
FY 97: $0

Populations Served: 300 volunteers with advanced HIV infection.

Constituency Involvement: Persons with HIV

Unmet Need: None.

Objective 2: Evaluate the cost-effectiveness of alternative strategies for preventing HIV-related opportunistic infections.

Action Steps: Embed clinical and cost data from randomized trials and observational cohorts into a comprehensive decision-analytic, cost-effectiveness model.

Descriptions: Cost-Effectiveness of Preventing AIDS Complications.

FY 95: $346,420
FY 96: $21,020
FY 97: $0

Populations Served: Persons with HIV.

Constituency Involvement: N/A

Unmet Need: None.

Agency: Department of Health and Human Services, Centers for Disease Control and Prevention

Goal: To more accurately monitor the HIV epidemic and provide data to assess and direct prevention programs by strengthening existing systems and develop new surveillance systems.

Objectives: Implement projects that evaluate and expand the uses of HIV infection and AIDS case surveillance and sero-surveillance data so that these data systems can more effectively guide public health policy and provide relevant information necessary to direct and evaluate prevention activities.

Improve understanding of the natural history of HIV infection as well as the risk factors and protective factors for sexual, drug-related, perinatal, and healthcare worker related HIV transmission in order to develop more effective prevention strategies for all affected populations.

Action Steps: Evaluate HIV infection reporting systems (named, anonymous, unique identifier) used nationally for their ability to monitor the epidemic, provide linkages to medical and social services, and to assess their impact on a person's decision to be tested.

Characterize high risk behaviors of persons with evidence of recent HIV infection such as persons with documented HIV seroconversion, high CD4+ counts, or diagnosis of HIV infection in adolescents.

Assess the impact of public health guidelines and recommendations and prevention efforts,

Characterize persons co-infected with TB and HIV.

Evaluate ways to improve the completeness and quality of risk ascertainment on persons reported with HIV and AIDS.

Identify and characterize previously unreported AIDS cases among deaths investigated by local medical examiners to assess the impact of under-diagnosis of AIDS cases on AIDS surveillance among disadvantaged populations that often do not receive adequate health care.

Test the efficiency of new techniques for reporting HIV and AIDS surveillance data from health care providers and laboratories to health departments.

Collect additional data on persons reported through HIV/AIDS

surveillance which may be important for the planning and evaluation of prevention and care programs, such as social/economic status, levels of disabilities, drug use history, sex behavior history, utilization of HIV testing and medical care services, and reproductive history in women.

Assess the interrelationship of behaviors, HIV markers and surrogates, and their potential role in surveillance systems.

Assess the interaction of socioeconomic, behavioral, and biologic factors in HIV transmission.

Determine the role of female-specific biological factors that are linked to acquisition and transmission of HIV infection and that influence the course of HIV disease.

Determine factors contributing to the efficiency of sexual transmission of HIV.

Assess the risk of transmission of HIV and TB from HIV-infected health-care worker to patient and vice versa.

Develop systems to monitor the emergence of multidrug-resistant TB in the HIV infected.

Continue to develop improved methods for projecting or modeling the HIV epidemic.

Develop methods to differentiate HIV-specific antibodies generated in participants in HIV vaccine trials from those generated in response to HIV infection.

Develop methods to identify potential cases of HCW-to-patient transmission.

Expand HIV reporting systems to collect information about primary and secondary HIV prevention services needed and received by HIV-positive clients (in collaboration with HRSA).

Work with providers and users of lab services to develop & implement systems which provide assurance that the capacity and quality requirements for HIV testing are met.

Work with international partners to study TB, implement vaccine trials, enhance clinical management, assess prevention efficacy, and improve program management of HIV/AIDS.

Develop methods to evaluate the use of HIV infection and AIDS

surveillance systems to assess early intervention strategies.

Descriptions: Many of the activities in the above-cited action steps are carried out through cooperative agreements with state and local health departments. In addition, specialized projects and studies also serve to focus attention on these activities, these include: Evaluation of HIV Infection Reporting Systems Project, Recent HIV Infection Projects, Surveillance to Evaluate Prevention Projects, Adult Spectrum of Disease Project, the TB Project, Mode of Transmission Validation Project, the Medical Examiner Study, and the Enhancement of AIDS Surveillance Efficiency Project.

FY 95: $141,046,000
FY 96: $139,668,000
FY 97: $139,778,000

Populations Served: All major racial, ethnic, and risk groups.

Constituency Involvement: There is regular consultation with national, state, and local public health officials and many other relevant organizations such as HIV-related community-based organizations.

Unmet Need: The current system does not provide for adequate surveillance of risk behaviors that contribute to HIV transmission, nor does it provide an accurate means for monitoring HIV incidence.

Agency: Department of Health and Human Services, Centers for Disease Control and Prevention

Goal: To increase the public understanding of, involvement in, and support for HIV prevention.

Objectives: Provide leadership in HIV and STD prevention by (1) establishing sustained and active national agenda through the media; (2) promoting credible messages based on science through credible channels; and (3) encouraging and supporting prevention efforts at the local level.

Establish a collaboration of partners composed of national, State, and local organizations to facilitate (1) diffusing social marketing principles applied to HIV and STD prevention at the local level; (2) identifying and promoting mechanisms to exchange technology and information; and (3) developing guidelines for applying social marketing principles to local HIV and STD prevention.

Apply social marketing principles at the local level for the purpose of (1) demonstrating the participatory social marketing process (i.e., skills and resources needed to effectively engage the community); (2) measuring the effects of behavior-based social marketing interventions; and, (3) documenting the lessons learned.

Facilitate the application of prevention marketing principles in CDC-funded community planning efforts by (1) promoting guidelines for consideration of these principles at the local level for prevention interventions and (2) providing interactive technical assistance on social marketing technology principles (or prevention marketing) to public health agencies as well as HIV Prevention Community Planning Groups.

Promote HIV prevention as a relevant issue in business settings.

Provide and promote a network of resources and referrals to assist in implementing the Business Responds to AIDS (BRTA) Comprehensive HIV/AIDS Workplace Program.

Market the comprehensive workplace HIV/AIDS program to business.

Establish and execute a research agenda to formulate and assess strategies and resources to advance the knowledge of effective workplace HIV programs.

Action Steps: Monitor changes in public knowledge about how HIV is and is not transmitted;

Develop methodologies to measure community mobilization or changes in institutional behavior in relation to mass media public information and education programs;

Develop new mass media messages, in collaboration with the public health systems and with international, national, state, and local private sector organizations and agencies;

Expand the relationship between CDC and the entertainment industry to improve messages and role modeling for HIV prevention;

Develop communication interventions with appropriate organizations to ensure that consistent, accurate HIV prevention information is provided to the public;

Develop community coalitions for HIV prevention;

Coordinate and disseminate information messages through the media that explain new scientific findings and policies concurrent with the release of new scientific information;

Develop leadership of health/education officials to effectively deliver HIV prevention messages through partnerships;

Evaluate the role of communications in changing individual knowledge, community norms, and individual behavior through establishment of model programs;

Expand the relationship between CDC and academic experts in mass communications to develop methods for measuring the impact of mass media on individual and community behaviors;

Develop ways of measuring the mobilization of community groups, i.e., changes in community norms, capacity;

Monitor business policies and employee education programs regarding HIV/AIDS;

Implement a BRTA initiative to develop HIV prevention and service programs for the workplace and the community;

Sponsor and participate in national meetings of businesses and religious, civic, medical, social, and voluntary agencies which conduct HIV prevention and service programs.

Descriptions: Many of the activities cited above are carried out at local demonstration sites and in coordination with community planning efforts. In addition, specialized projects and studies

also serve to focus attention on these activities, these include projects entitled: National Health Communications, Prevention Collaborative Partners, the CDC National AIDS Clearinghouse, and the CDC National AIDS Hotline, and the Prevention Marketing Initiative.

Also, linkage efforts with business, labor, and community groups have received special attention. The Business Responds to AIDS (BRTA) and Labor Responds to AIDS (LRTA) programs have focused on issues such as: HIV/AIDS workplace policies, supervisor and labor leader training, employee education, employee family education, and community service and volunteerism. Partnerships have also been forged among a variety of communities including business, labor, religious, voluntary and the media. And, national and regional minority organizations have also been sought out in forging these important linkages.

FY 95: $45,960,000
FY 96: $45,512,000
FY 97: $45,547,000

Populations Served: All segments of the population including all major racial and ethnic groups, young persons (18-25), persons engaging in behaviors that place them at risk for HIV infection, and business and labor leaders including their employees and families.

Constituency Involvement: Regular consultation with leaders from over 200 prevention collaborative partners composed of national, state, and local organizations and over 50 business and labor partners.

Unmet Need: There is a need for more effective use of social marketing principles in HIV prevention programs, further implementation of strategies to promote adoption of BRTA and LRTA comprehensive programs. There is also an increased need for family education materials, more effective materials to encourage abstinence and other prevention behaviors, and more HIV prevention materials for use by religious communities.

Agency: Department of Health and Human Services, Centers for Disease Control and Prevention

Goal: To prevent risk behaviors that can cause HIV infection and related health problems in school age children and college age youth through implementation of comprehensive school health education programs.

Objectives: Increase by 15 percent the proportion of school districts that require age-appropriate HIV education at each grade level, K-12, especially at grades 9-12, preferably as part of comprehensive school health education.

Increase by 15 percent the proportion of colleges and universities that provide HIV education for students and staff, preferably as part of an institution-wide health promotion program.

Decrease by 10 percent at each grade level the proportion of 9th to 12th grade students who report they have engaged in sexual intercourse.

Among 9th to 12th grade students who report they have engaged in sexual intercourse, decrease by 10 percent the proportion who report they have engaged in sexual intercourse during the past 3 months.

Among 9th to 12th grade students who report they have engaged in sexual intercourse during the past 3 months, increase by 10 percent the proportion who report they used a condom at last intercourse.

Decrease by 10 percent the proportion of 9th to 12th grade students who report they have injected illicit drugs.

Action Steps: Monitor state-level policy and program requirements that support effective HIV education within comprehensive school health education (CSHEs);

Monitor district-level policy and program requirements that support effective HIV education within comprehensive school health education programs;

Monitor the prevalence of behaviors that cause HIV infection and related health problems among school and college youth;

Implement and revise as necessary, CDC guidelines for effective school health education to prevent the spread of HIV infection;

Enhance the capacity of state and local educational agencies to

develop and implement effective HIV education within CSHEs;

Enhance the capacity of colleges and universities to provide HIV education for students and staff, preferably as part of an institution-wide health promotion program;

Ensure the integration of education to prevent HIV infection, other STDs and the use of alcohol and other drugs among youth;

Strengthen the capabilities of state and local departments of education and health to collaboratively help schools, colleges and universities implement effective HIV education programs for youth;

Increase the effectiveness of HIV education for youth served by state and local departments of education and colleges and universities through the efforts of selected national organizations;

Enhance the capacity of state and local agencies to help prevent HIV infection and HIV-related problems among youth through the efforts of training and demonstration centers established for state and local departments of education;

Establish teacher training coordinators in every interested state to help teachers provide effective HIV education within a CSHE;

Identify and disseminate, through training and demonstration centers and through teacher training directors, HIV education programs that have been shown to the be effective in reducing behaviors that cause HIV infection and related health problems;

Synthesize and apply the results of research to increase the effectiveness of HIV prevention education for youth;

Conduct formative evaluations of state and local departments of education policies, curricula, teacher training, and school efforts to prevent behaviors that cause HIV infection and related health problems;

Develop a standardized report for each state to profile the nature of priority health problems and risk behaviors among youth in that state and school efforts to prevent these problems and behaviors;

Conduct evaluations of the effectiveness of existing school-based interventions to reduce behaviors that result in HIV infection and related health problems;

Develop state-of-the-art school-based interventions and evaluate

their effectiveness in reducing behaviors that result in HIV and related health problems; and

Conduct and apply meta-evaluations of existing research data about the effectiveness of school-based interventions in reducing health risks behaviors among adolescents.

Descriptions: Funding and technical assistance for state and local educational agencies is provided through several avenues including national non-governmental organizations, colleges and universities, and teacher training sites. There is also support for youth surveys and projects to reach out-of-school youth.

FY 95: $48,205,000
FY 96: $47,735,000
FY 97: $47,771,000

Populations Served: Young persons engaging in behaviors that place them at risk for acquiring HIV through sexual exposure, including all major racial and ethnic groups. All school- and college-aged youth regardless of school enrollment status.

Constituency Involvement: Consultation with a wide range of constituency groups was established to: (1) improve existing programmatic efforts; (2) improve assistance and resources provided by CDC; and, (3) explore strategies that the Nation might take to improve the health status of young people. These groups include representatives from: (1) every state education agency, District of Columbia, and six territorial education agencies; (2) national nongovernmental health or education organizations, 3) colleges and universities, 4) state public health departments, as well as young people themselves. Meetings included an annual constituency meeting, quarterly training programs, and communication through an electronic bulletin board and network.

Unmet Need: Not all youth are accessible through existing institutional-based efforts, and currently not all states monitor youth health-risk behaviors.

Agency: Department of Health and Human Services, Centers for Disease Control and Prevention

Goal: To prevent or reduce behaviors or practices which place individuals at risk of HIV infection, and for HIV positive individuals, place others at risk.

Objectives: At least 90 percent of individuals with known HIV infection will be abstinent or will have used a condom at last sexual intercourse, and at least 50 percent of individuals who have engaged in high-risk sexual behaviors within the past 12 months will be abstinent, in a mutually monogamous relationship, or have used a condom at last sexual intercourse.

At least 75 percent of injecting drug users will have stopped injecting drugs or used sterile or decontaminated injection equipment at last injection.

At least 80 percent of the health care and public safety workplaces will implement programs and procedures for preventing HIV transmission at work sites.

Reduce unintended pregnancies to no more than 40 percent of pregnancies among women with or at risk for HIV infection.

The number of individuals donating blood and found to be infected with HIV at the time of donation will decrease by 50 percent through self-deferral.

Among selected populations of youth in high-risk situations, increase by 10 percent the proportion who report they used a condom at last sexual intercourse.

Action Steps: Collaborate with prevention partners to assess risk behaviors and practices in selected communities;

Identify barriers to implementation of HIV prevention programs at community, state, and national levels;

Collaborate with selected communities in developing and implementing a model behavioral intervention program that comprehensively addresses community needs and uses available community resources and prevention partners in selected sites;

Design, develop, and test effective community-level interventions to change risk behaviors through altering community norms and values to support healthy behaviors;

Expand the community's capacity to plan, implement, and evaluate culturally competent and linguistically specific HIV prevention guidelines and programs tailored to the needs of specific populations;

Enhance the capacity of CDC staff to plan, administer, and evaluate behavioral change strategies and community-based interventions to provide public health leadership and assist our prevention partners in designing and managing effective strategies for HIV prevention programs;

Enhance the capacity of local health departments and other relevant community agencies to collaboratively provide effective HIV education for youth in high-risk situations;

Establish scientifically-based evaluation components for HIV prevention activities; and

Use evaluation of components to design or refine HIV prevention programs and/or redirect HIV prevention resources.

Descriptions: Several mechanisms are employed for achieving the goals and objectives cited above. These include cooperative agreements with state and local health departments, in addition to direct funding of community-based organizations, national organizations, and national minority organizations. HIV intervention research studies are also supported.

FY 95: $185,625,000
FY 96: $183,814,000
FY 97: $203,958,000

Populations Served: All major racial and ethnic groups in addition to persons engaging in behaviors that place them at risk for acquiring HIV.

Constituency Involvement: A major avenue for constituency involvement is the HIV Prevention Community Planning Process. Through this mechanism, state and local health departments form community planning groups to assist in developing HIV prevention plans. In addition, there is regular and extensive consultation with representatives from state and local health departments, community planning groups, and national organizations.

Unmet Need: There is currently a lack of behavioral risk surveillance data for program planning and evaluation purposes. There is also a need to develop a more effective application of behavioral science findings to HIV prevention programs. And there

is a special need to develop and maintain prevention efforts that target high risk women, youth and gay men of color.

Agency: The Department of Health and Human Services, Centers for Disease Control and Prevention

Goal: To increase individual knowledge of serostatus and strengthen systems for successful referral to early intervention services.

Objectives: At least 85 percent of the estimated 800,000 to 1,000,000 HIV-infected individuals will know their HIV serostatus.

At least 90 percent of health care sites receiving public funds and serving at-risk persons will provide appropriate HIV counseling and testing services.

At least 80 percent of known HIV infected individuals, either directly or through referral, will receive primary and secondary prevention services.

Action Steps: Working with governmental and nongovernmental partners, enhance community-level assessments of needed primary and secondary prevention services;

Identify opportunities for common HIV prevention data collection and development of uniform data sets;

Integrate HIV prevention services into standards of care for the diagnosis and treatment of HIV disease;

In collaboration with the FDA, develop, test, and implement rapid HIV testing procedures;

Strengthen the capacity of state, and local health departments to provide partner notification services to private health care providers offering HIV counseling & testing;

Develop alternative methods to provide HIV counseling and testing services;

Work with professional groups, hospitals, and state health departments to ensure that health care workers receive adequate training on primary and secondary HIV prevention (in collaboration with HRSA);

Study the impact of discrimination as a barrier to prevention services;

Assist publicly funded counseling and testing sites establish selection criteria and systems for monitoring the quality of referral laboratories;

Interview persons newly diagnosed with HIV infection to identify missed opportunities for earlier diagnosis and CD4+ testing;

Conduct a study of incident AIDS cases to determine what services HIV-positive clients are receiving over time to identify service gaps (in collaboration with HRSA); and

Provide guidelines and training to HIV counselors to improve the quality of counseling.

Descriptions: Counseling, testing, referral partner notification programs are supported as part of cooperative agreements with state and local health departments.

FY 95: $168,995,000
FY 96: $167,351,000
FY 97: $181,027,000

Populations Served: All major racial and ethnic groups and persons engaging in behaviors that place them at risk for acquiring HIV.

Constituency Involvement: A major avenue for constituency involvement is the HIV Prevention Community Planning Process. Through this mechanism, state and local health departments form community planning groups to assist in developing HIV prevention plans. In addition, there is regular and extensive consultation with representatives from state and local health departments, community planning groups, and national organizations.

Unmet Needs: There is a need for more effective long-term intervention programs for HIV positive individuals in addition to a lack of resources for supporting comprehensive referral and data monitoring systems. Also, there is a need to determine the best balance between CTRPN programs and other HIV prevention strategies.

Agency: Department of Health and Human Services, Food and Drug Administration

Goal: To reduce transfusion-transmitted HIV infection.

Objective: Ensure supply and safety of the national blood supply.

Action Steps: Establish policies, expedite review of product applications, conduct approval inspections, oversee surveillance, and support enforcement activities.

Descriptions: Encourage high risk donors to exclude themselves; update list of unsuitable donors; quarantine and test blood; investigate incidents to identify, and rectify common errors in blood banks.

FY 95: $17,458,000
FY 96: $17,458,000
FY 97: $17,458,000

Populations Served: All persons who may receive blood or blood products.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Unmet Need: With the passage of Prescription Drug Use Fee Act of 1992, the FDA has been able to expeditiously review HIV/AIDS related therapeutic applications. With the continuation of the provisions in the Act, the FDA will be able to continue expeditious reviews.

Agency: Department of Health and Human Services, Health Care Financing Administration

Goal: To reduce perinatal transmission among Medicaid-eligible women.

Objectives: Develop and implement a campaign to inform HIV positive women in selected pilot areas about the benefits of AZT in FY 95.

Expand pilot project to one State in all regions in FY 96.

Expand project to include all States in FY 97.

Action Steps: Develop, obtain, and distribute brochures and other materials describing current guidelines for the use of AZT during pregnancy for preventing perinatal transmission, and Medicaid eligibility and coverage to Medicaid eligible women.

Descriptions: Establish a consumer-oriented educational campaign in key states with high HIV prevalence rates among women.

FY 95: $50,000 (Federal share)
FY 96: $60,000 (Federal share)
FY 97: $185,000 (Federal share, subject to availability of funds)

Populations Served: HIV positive women eligible for Medicaid coverage.

Constituency Involvement: Significant consultation with high-risk pregnant women and their advocates.

Unmet Need: The pilot project will not initially include women of unknown or negative HIV serostatus.

Agency: Department of Health and Human Services, Health Resources and Services Administration

Goal: To reduce the perinatal transmission of HIV.

Objective: Enhance provider capacity to provide appropriate services for women at the community level.

Improve provider capacity for outreach, counseling, testing and care for women of childbearing age for early identification and linkage to care for pregnant women.

Enhance providers' abilities to provide AZT for HIV positive pregnant women.

Ensure funding and dissemination of innovative models of care that evaluate all of the major care and service goals listed in this plan: effectively educated providers, increased access to and quality of care, reduction of perinatal transmission of HIV.

Action Steps: Establish the Women's Initiative for HIV Care for Women and Reduction of Perinatal Transmission (WIN);

Establish ongoing WIN Steering Committee;

Provide technical assistance to grantees;

Conduct centralized training for all WIN sites with follow-up local training;

Collaborate with Association of Maternal & Child Health Programs (AMCHP) to develop local guidelines;

Establish MCHB working group to coordinate HIV risk reduction related efforts across programs;

Distribute counseling and testing guidance, AHCPR consumer brochure and video, and other PHS documents to MCHB community;

Review currently funded SPNS projects to identify gaps in project coverage for future Requests for Applications (RFAs); and

Evaluate sites.

Descriptions: Enhance outreach for HIV counseling and testing.

Improve service linkages for women of childbearing age in an ongoing care system and to reduce perinatal HIV transmission.

PHS 076 Implementation Plan.

FY 95: $1,520,000
FY 96: $1,800,000
FY 97: $1,890,000

Populations Served: CARE Act grantees. Adolescent and adult women and their infants, with special attention for pregnant women in addition to MCH and HIV providers.

Constituency Involvement: Health care providers, evaluation researchers, communication experts, and patient advocates. There is also consumer participation in WIN steering committee and projects advisory boards in addition to linkages with other HRSA grantees including those from RWCA and SPNS programs.

Unmet Need: Funds needed to provide more services in order to reach more women and enhance evaluation efforts and improve technical assistance and training.

In particular, it is critical to fund services (e.g., outreach, case finding, case management) that better link women of childbearing age with counseling and testing services and, after testing, with comprehensive medical, social, and support services and long-term followup for themselves and their families. Training non-HIV providers, particularly primary care, family practice, ob/gyn, and MCH providers, to perform women-sensitive counseling and testing, to deliver appropriate primary care for women with HIV, and to provide appropriate referrals for these women is another critical need. Funding is also needed for peer-support programs for these women and their families. While it should be our assumption that all women are at risk for HIV, it is important to recognize that certain groups of women (e.g., substance abusers, partners of substance abusers) are at special risk and need additional services in order to enter and remain in care.

Agency: Department of Health and Human Services, Indian Health Service

Goal: To reduce the number of new infections among federally recognized American Indians and Alaska Natives.

Objective 1: Maintain surveillance of HIV infection in American Indians and Alaska Natives.

Action Steps: Maintain timely and complete case reporting to appropriate local, state and national entities and the Indian Health Service (IHS) AIDS Prevention Activities Office.

Descriptions: Area AIDS Coordinators will be responsible for reporting.

FY 95: $ 912,000
FY 96: $ 912,000
FY 97: $1,800,000

Populations Served: Federally recognized American Indians and Alaska Natives.

Constituency Involvement: Local and National Indian Health Advisory Boards.

Unmet Need: Increased staff and resources would permit expansion of prevention activities.

Objective 2: Maintain training and information activities to provide health education and risk reduction messages.

Action Steps: Teach empowerment skills at the individual and community level that will enhance the individual's ability to actualize assimilated knowledge as behavior change.

Descriptions: HIV health education and risk reduction message dissemination.

FY 95: Part of overall IHS budget.
FY 96: Part of overall IHS budget.
FY 97: Part of overall IHS budget.

Populations Served: American Indians and Alaska Natives population, tribal leaders, women, youth, individuals practicing high risk behavior, and IHS/tribal health care workers.

Constituency Involvement: Local and National Indian Health Advisory

Boards.

Unmet Need: Increased staff and resources would permit expansion of prevention activities.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To conduct and support behavioral and social science research to further understanding of the determinants and processes that influence behaviors associated with HIV transmission and to develop and improve HIV prevention intervention strategies, and, to conduct and support natural history and epidemiological research to improve the understanding of the risk factors and mechanisms of HIV transmission and disease progression and to develop prevention strategies to reduce or prevent HIV transmission.

NIH's efforts in these areas can be found in Appendix B: Research.

Agency: Department of Health and Human Services, Office of Population Affairs

Goal: To reduce the number of new HIV infections.

Objective: Provide counseling, education, and HIV testing as needed to Title X program clinics.

Action Steps: Include HIV/AIDS education in all clinic education programs.

Include HIV/AIDS prevention in STD screening programs.

Provide HIV testing or referral for testing to all Title X clients who request testing.

Descriptions: Title X Program

FY 95: NA -- HIV services integrated into overall budget.
FY 96: NA -- HIV services integrated into overall budget.
FY 97: NA -- HIV services integrated into overall budget.

Populations Served: The Title X program provides family planning and related reproductive health services to approximately 4.5 million clients annually through a network of 4,500 clinics. Clients are predominantly young women; most are members of low-income families, and 30 percent are adolescents and 33 percent are below age 25.

Constituency Involvement: For non-profit grantees, clients participate on boards of directors. For all grantees, clients participate on committees approving all information and education materials.

Unmet Need: The Title X program reaches an estimated 50 percent of potential clients. Expansion of program would provide a concomitant expansion in HIV/AIDS prevention activities, since these are provided as an integral part of the reproductive health services in Title X programs.

Agency: Department of Health and Human Services, Substance Abuse and Mental Health Services Administration

Goal: To reduce the number of new HIV infections.

Objective: Demonstrate the effectiveness of incorporating HIV/AIDS prevention curricula into ongoing substance abuse prevention programs.

Demonstrate the differential effectiveness of incorporating HIV/AIDS prevention curricula into ongoing substance prevention programs.

Action Steps: Supplementation of high risk youth grants for alcohol, tobacco and other drugs (ATOD) prevention for the purpose of including HIV/AIDS prevention strategies in their present activities.

Develop program to empower youth with skills, knowledge, and beliefs for HIV prevention.

Demonstrate effective strategies to prevent ATOD use and abuse among high risk youth.

Include developmentally and culturally appropriate HIV/AIDS education and prevention approaches.

Descriptions: High Risk Youth Program.

FY 95: $292,000
FY 96: $0
FY 97: $0*

* In addition, SAMHSA's Knowledge Development Application (KDA) Program includes an AIDS initiative in FY 1997. This initiative includes various approaches, including how best to: educate service providers, address family issues, interrupt HIV transmission, and maximize client retention in substance abuse treatment. The FY 1997 estimate for HIV/AIDS in the President's Budget is $15,000,000.

Populations Served: High risk youth or youth at risk for ATOD, adolescent females, and youth at risk for AOD-related violent behavior.

Constituency Involvement: Families of youth, youth service workers, and the communities that support youth at risk for ATOD abuse.

Unmet Need: Presently this initiative reaches only 25 percent of high risk youth grantees. Supplementing all grantees would provide greater opportunity for services integration and evaluation.

Agency: Department of Housing and Urban Development

Goal: To reduce the number of new infections among residents of public and subsidized housing.

Objective: Provide primary prevention programs to public housing residents at risk for HIV infection. Coordinate meetings of the state and local agencies responsible for the prevention program services.

Action Steps: Forge local partnerships and improve coordination of existing resources.

Descriptions: HIV/AIDS Prevention in Public Housing Demonstration Program.

FY 95: $0 (Activities carried out within existing HUD personnel resources.)
FY 96: $0 (Activities carried out within existing HUD personnel resources.)
FY 97: $0 (Activities carried out within existing HUD personnel resources.)

Populations Served: Children and adults in public housing in five targeted cities.

Constituency Involvement: Input received through local planning groups.

Unmet Need: The initial demonstration program reached sites in five cities. An increase in resources would enable HUD to meet increasing demand for services and permit expansion to include other public and subsidized housing efforts.

Agency: Department of Justice

Goal: To reduce risk of infection of infection to INS detainees who are at risk.

Objective: Educate detainees believed to be at risk regarding HIV/AIDS and thereby reduce the risk of transmission and new infections.

Action Steps: Upon obtaining informed consent, test detainees suspected of or diagnosed with HIV/AIDS or test upon detainee request and provide pre- and post-test counseling to detainees deemed at risk.

Descriptions: Provide limited testing and counseling.

FY 95: Part of overall operating budget.
FY 96: Part of overall operating budget.
FY 97: Part of overall operating budget.

Populations Served: INS Detainees.

Constituent Involvement: None.

Unmet Need: None.

Agency: Department of Justice

Goal: To reduce the risk of employee infection and avoid possible worksite performance problems.

Objective: Educate Bureau of Prisons (BOP) staff, Drug Enforcement Agency (DEA) employees, Federal Bureau of Investigation (FBI) employees, Immigration and Naturalization Service (INS) employees, and U.S. Marshals Service (USMS) regarding HIV/AIDS transmission and thereby reduce the risk of infection. Educate all Justice Department employees about HIV/AIDS in the workplace.

Action Steps: For Bureau of Prison (BOP) staff provide: annual HIV information update and infectious disease training to all staff; produce inmate and staff HIV educational videos; and participate at least quarterly with HRSA in audio conferences on HIV issues.

For DOJ employees in occupations that possess a heightened possibility for exposure to HIV or other bloodborne pathogens, including employees of the DEA, FBI, INS, and USMS provide: general training and field office training; annual bloodborne pathogen training to all personnel as mandated by OSHA (discussion of HIV/AIDS is included in this training); and an annual update on the bloodborne pathogens training as necessary to discuss new information or changes in the use of safety equipment, etc.

For all Department employees, the Justice Management Division (JMD) provides: instructional materials to be used in a one time general training; and technical assistance to other DOJ components.

Descriptions: DOJ staff prevention training programs.

FY 95: Part of overall operating budget.
FY 96: Part of overall operating budget.
FY 97: Part of overall operating budget.

Populations Served: DOJ employees.

Constituency Involvement: None.

Unmet Need: Additional resources for field office training for USMS and FBI.

Agency: Department of Veterans Affairs

Goal: To prevent transmission of HIV infection through education of employees and patients.

Objective 1: Train and maintain cadre of professional staff to conduct HIV transmission and prevention education for patients and conduct pre- and post-test HIV antibody test counseling.

Action Steps: Establish national training program to educate two professional staff from every VA medical center to conduct patient education and pre- and post-test counseling.

Maintain on-going training program on limited basis to address turnover of staff and maintain cadre of counselors/patient educators.

Objective 2: Educate and maintain cadre of knowledgeable staff to teach all staff in VA health-care facilities on prevention and transmission of HIV infection.

Action Steps: Develop a national "train the trainer" education program to educate selected staff from every VA Medical Center on how to organize and conduct staff educational activities on HIV transmission and prevention.

Update training materials/revise strategies to maintain knowledgeable base of trainers for every facility.

Objective 3: Integrate HIV prevention education in addiction treatment programs.

Action Steps: Conduct national training program for professional staff in addiction treatment programs and Vet Centers on how to integrate HIV prevention education for patients in their treatment areas.

Objective 4: Stimulate innovative approaches to HIV/AIDS education at the local level (VA Medical Centers and communities).

Action Steps: Award educational demonstration grants to HIV/AIDS education proposals on competitive basis.

Facilitate system-wide dissemination of completed projects through annual publication and national quarterly newsletters.

Objective 5: Maintain education and information support systems.

Action Steps: Continue AIDS awareness and education programs through national system of regional education centers and individual facility programs.

Through library system, continue purchase of appropriate private and Federal sector videos, publications, posters, and other materials.

Objective 6: Prevent transmission of HIV in health-care setting.

Action Steps: Ensure on-going implementation of CDC recommendations on universal precautions, via policy.

Ensure continuing implementation of OSHA rule on protection of health-care workers against bloodborne pathogens via policy.

Provide national training program on interdisciplinary team training for staff from infection control, employee health, safety in all VAMCs to implement OSHA rule.

Descriptions: Prevention activities including education and universal precautions.

FY 95: $31,000,000 *
FY 96: $31,000,000 *
FY 97: $31,000,000 *

* Figures are based on the estimated resource expenditures for universal precautions and education and are part of the general Medical Care Budget. FY 1996 and FY 1997 estimates are based on the resource levels contained in the President's budget.

Populations Served: Eligible veterans through local medical centers and facilities, local VA health-care and support staff, veteran patients and families, general public.

Constituency Involvement: VA medical centers and health-care facilities, and local communities.

Unmet Need: Advances in treatment through research and/or changes in prevention activities may require re-assessment of funding levels.

Agency: Corporation for National Service

Goal: To offer HIV/AIDS education programs and other services with volunteers from the Learn and Serve America project.

Objective: Support HIV-related Learn and Serve America projects.

Action Steps: Continue programs for youth in elementary school or high school to volunteer in community service activities, such as peer education in HIV/AIDS prevention.

Continue to award higher education grants directly to colleges and universities which provide service opportunities on HIV/AIDS prevention.

Program Description: Examples of higher education programs include Robert Wood Johnson Medical School and the University of San Diego where students provide education on HIV/AIDS to homeless and other high risk populations.

FY 95: Part of overall operating cost.
FY 96: Part of overall operating cost.
FY 97: Part of overall operating cost.

Populations Served: Persons living with HIV and AIDS and others who could benefit from HIV/AIDS education.

Constituency Involved: The Learn and Serve America program and students across the country.

Unmet Needs: Without these programs, students would not have an opportunity to serve their communities in HIV/AIDS related projects.

Appendix B

Current Federal Activities

RESEARCH

Agency: **Department of Commerce**

Goal: To foster, serve, and promote the Nation's economic development and technological advancement, including encouraging HIV-related advances and innovation through the Department's collaborative efforts with the global business community.

Objective:

Support activities which can assist in forwarding AIDS research by expanding the role of public-private partnerships in developing a vaccine and therapeutics.

Action Steps: Through the Advanced Technology Program (ATP), promote advances in biotechnology and provide funding to small and start-up research and development companies.

Support the Patent and Trademark Office's (PTO) AIDS-related patent database, developed in partnership with the National Science Foundation.

Through the National Technical Information Service, disseminate HIV-related training and technical materials.

Through data collection and analysis programs conducted by the Bureau of the Census and the Bureau of Economic Analysis, provide data for decision-making regarding the distribution of funds and other resources for private and public health initiatives, including HIV-related research, treatment, and service programs.

Through scientific standards, methodologies and technologies developed through the programs of the National Institute of Standards and Technology, set standards for laboratory procedures and equipment calibration at research facilities, including those conducting HIV-related research.

Through the Patent and Trademark Office Biotechnology Examining Groups, review applications for a range of proposed HIV-related patents.

Descriptions: Advanced Technology Program, Patent and Trademark Office reviews, National Technical Information Service, Bureau of the Census, and the National Institute of Standards and Technology.

Resources:

FY 95: Part of overall operating budget

FY 96: Part of overall operating budget

FY 97: Part of overall operating budget

Populations Served: Start-up companies, biotechnology and pharmaceutical companies, academic institutions, and researchers.

Constituency Involvement: The Department supports public-private partnerships to encourage innovative research.

Agency: Department of Defense

Goal: To carry out state-of-the-art research on the prevention and treatment of HIV infection to promote medical readiness in U.S. military forces.

Objectives:

Support the development of a safe and effective HIV vaccine.

Support the development of new biochemical and genetic strategies to slow HIV disease progression

Support natural history studies for the purpose of evaluating the efficacy of intervention strategies.

Action Steps: Define the global molecular epidemiology of HIV to assist with candidate vaccine selection.

Explore novel vaccine technologies.

Conduct vaccine trials in endemic areas.

Assess the immune response and efficacy of vaccine candidates.

Evaluate potential therapies for treatment of HIV infection and potential for immune reconstitution.

Evaluate prevalence of drug resistance, develop rapid genetic assay for resistant mutants, and methods for genetic targeting of novel therapies *in vivo.*

Participate in national surveillance of AZT resistance.

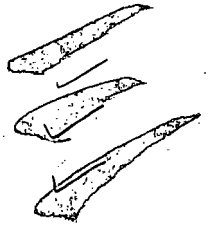
Develop a comprehensive panel of immunologic, virologic, and functional parameters for management of HIV infection.

Support natural history studies and specimen repositories.

Descriptions: Vaccine, therapeutic, and epidemiological research, including vaccine design, development and testing in the U.S. and overseas locations; epidemiologic studies of vaccine field studies; and conclusion of drug treatment and behavior studies.

Resources:

FY 95: ~~$38,494,000~~ e 38.5 million
FY 96: ~~$25,428,000~~ e 25.4 million
FY 97: ~~$ 9,611,000~~ e 9.6 million



Populations Served: Active duty personnel.

Constituency Involvement: Clinicians, researchers, and active duty personnel.

Agency: Department of Energy

Goal: To provide infrastructure support for physical chemical research, termed structural biology, including indirect support for HIV-related research.

Objective:

In collaboration with other Federal agencies, provide access to sophisticated equipment and specially trained scientific personnel.

Action Steps: In collaboration with all relevant agencies (NIH, NSF) and the scientists they support, provide continued essential support for structural chemistry and biology facilities. Provide both the academic and the industrial community access to the facilities for further studies on the structural biology of HIV.

Descriptions: The National Synchrotron Light Source at Brookhaven National Laboratory includes a Department of Energy (DOE) supported x-ray beam line extensively used by structural biologists studying virus structure, including the structure of HIV. In addition, through its National Laboratory system, DOE provides user facilities at other synchrotron light sources and at neutron beam facilities, which can be used by researchers to characterize the structural configuration of intact HIV, and HIV's biochemical components, often in complexes with inhibitors. These studies assist in the development of novel therapies, as well as advance our understanding of the pathogenesis and fundamental biology of HIV growth.

Resources:

FY 95: Part of DOE's general operating budget.

FY 96: Part of DOE's general operating budget.

FY 97: Part of DOE's general operating budget.

Populations Served: The scientific community.

Constituency Involvement: Access to resources through peer review.

Agency: Department of Health and Human Services, Agency for Health Care Policy and Research

Goal: To provide national estimates of the cost and use of HIV-related medical and non-medical services.

Objective 1:

To provide comprehensive information on unmet needs for service and barriers to accessing services.

To examine effects of different systems of organizing and delivering care on outcomes such as cost, utilization, survival, patient satisfaction, and quality of life.

Agency for Health Care Policy and Research, continued

To examine effects of patient characteristics (including gender, race/ethnicity, substance abuse, mental health, socioeconomic status, insurance coverage) on outcomes such as service utilization, unmet service needs, and costs.

To provide data on service utilization and costs for a representative sample of rural residents with HIV infection.

To examine patterns of transition between different types of provider (e.g., private physician to public clinic) and the relationship of such transitions to changes in clinical status, employment, and insurance coverage.

Action Steps: This study will be the first to obtain a true national random sample of people with HIV infection receiving treatment. Approximately 3200 adult patients in urban and rural areas will be enrolled. Study will be co-sponsored by HRSA, NIMH, NIDR, NIA, NIDA, and the Robert Wood Johnson Foundation.

Descriptions: HIV Costs and Service Utilization Study (HCSUS).

Resources:

FY 95: ~~$4,150,657~~ 4.1 million
FY 96: ~~$3,468,114~~ 3.5 million
FY 97: ~~$3,131,582~~ 3.1 million

Populations Served: HIV-infected individuals receiving treatment.

Constituency Involvement: A Community Advisory Board, comprising members of infected and affected groups, has been established.

Objective 2:

To examine health care utilization among participants in the NIH-sponsored Women's Interagency HIV Study (WIHS).

Action Steps: Supplement the WIHS by adding a health services research component.

Collect and analyze utilization data on women with HIV infection (in addition to the detailed clinical data obtained in the core study.)

Descriptions: Women's Interagency HIV Study (WIHS).

Resources:

FY 95: $60,000
FY 96: $0
FY 97: $0

Populations Served: Women with HIV infection participating in the WIHS.

Constituency Involvement: A broad representation of researchers and patient advocates had input in the development of the WIHS.

Agency for Health Care Policy and Research, continued

Objective 3:

To examine factors affecting health care utilization among participants in the NIH-sponsored Multicenter AIDS Cohort Study (MACS).

Action Steps: Supplement the MACS by adding a health services research component.

Collect and analyze utilization data on men with HIV infection (in addition to the detailed clinical data obtained in the core study).

Descriptions: Multicenter AIDS Cohort Study (MACS).

Resources:

FY 95: $65,000

FY 96: $0

FY 97: $0

Populations Served: Homosexual and bisexual men participating in the MACS in four urban areas.

Constituency Involvement: A broad representation of researchers and patient advocates had input in the development of the MACS.

Objective 4:

To examine health care utilization among participants in the CDC-sponsored HIV Epidemiological Research Study (HERS).

Action Steps: Supplement the HERS by adding a health services research component.

Collect and analyze utilization data on women with HIV infection (in addition to the detailed clinical data obtained in the core study).

Descriptions: HIV Epidemiological Research Study (HERS).

Resources:

FY 95: $50,000

FY 96: $50,000

FY 97: $50,000

Populations Served: Women with HIV infection participating in the HERS.

Constituency Involvement: A broad representation of researchers and patient advocates had input in the development of the HERS.

Objective 5:

To provide longitudinal data on utilization of inpatient, outpatient, home care, pharmaceutical, and other services, and to estimate their associated costs.

To examine the impact of a Medicaid Home and Community-Based waiver on service utilization, costs, functional status, and survival.

To examine any substitutions of formal for informal home care.

Agency for Health Care Policy and Research, continued

Action Steps: Conduct interviews with participants in New Jersey Medicaid Waiver program. Abstract data from Medicaid claims.

Descriptions: Health Care Costs and Utilization in AIDS Home Care.

Resources:

FY 95: $295,918

FY 96: $39,456

FY 97: $0

Populations Served: Medicaid recipients with AIDS in New Jersey.

Constituency Involvement: Persons with AIDS residing at home or in community facilities.

Objective 6:

To examine types of ambulatory care providers used to treat HIV infection, patterns of transitions between ambulatory provider types, and service utilization and costs for pediatric HIV patients.

Action Steps: Analyze Medicaid claims and eligibility data from New York State Medicaid files.

Descriptions: Ambulatory Care for HIV/AIDS, Models and Outcomes.

Resources:

FY 95: Part of overall operating budget.

FY 96: Part of overall operating budget.

FY 97: Part of overall operating budget.

Populations Served: New York State Medicaid recipients.

Constituency Involvement: NA

Objective 7:

To assess the impact of antiretroviral, antimicrobial, and prophylactic treatment on the natural history of HIV infection, and the effect of pharmaceutical therapies on service utilization, costs, and clinical outcomes.

Action Steps: Develop clinical database linked to Medicaid claims data.

Descriptions: Outcomes of Pharmaceutical Therapy in HIV Disease.

Resources:

FY 95: $527,497

FY 96: $479,952

FY 97: $505,000

Populations Served: HIV-infected population in Maryland.

Constituency Involvement: NA

Agency for Health Care Policy and Research, continued

Objective 8:

To study issues of costs and quality of care, with a focus on women and children, examine trends and variation in adherence to scientifically-based clinical guidelines, and study predictors of variation in treatment, by patient, physician, and practice setting characteristics.

Action Steps: Analyze Medicaid claims and eligibility data, supplemented with AIDS Registry data.

Descriptions: Quality and Costs of Care for HIV Infected Medicaid Patients.

Resources:

FY 95: Part of overall operating budget.

FY 96: Part of overall operating budget.

FY 97: Part of overall operating budget.

Populations Served: New Jersey Medicaid recipients.

Constituency Involvement: NA

Objective 9:

To develop an econometric framework for the simultaneous study of health care usage and survival, and synthetic estimates of per-person lifetime costs of HIV disease for various groups of HIV-infected individuals.

Action Steps: Formulate statistical models and associated computer software.

Descriptions: Developing Econometric Models to Estimate AIDS Costs.

Resources:

FY 95: $248,126

FY 96: $8,003

FY 97: $0

Populations Served: Participants in the AIDS Costs and Service Utilization Survey, with potential extensions to all persons with HIV disease.

Constituency Involvement: NA

Objective 10:

To identify personal and institutional factors that shape physicians' willingness to care for HIV-infected patients.

Action Steps: Conduct the third in a series of interviews with physicians, who are currently in their sixth post-graduate year.

Descriptions: Determinants of Physicians' AIDS-Related Practice Behavior.

Resources:

FY 95: Part of overall operating budget.

FY 96: Part of overall operating budget.

FY 97: Part of overall operating budget.

Agency for Health Care Policy and Research, continued

Populations Served: Persons with AIDS.

Constituency Involvement: Physicians

Objective 11:

Continuing work previously completed with AHCPR support, compare outcomes of inpatient care for AIDS provided by dedicated AIDS units versus scattered-bed approaches.

Action Steps: Expand upon original comparative multi-site observational study of 20 hospitals.

Descriptions: Outcomes of Hospital Dedicated AIDS Units.

Resources:

FY 95: $180,649

FY 96: $214,708

FY 97: $0

Populations Served: 1300 patients receiving services in study hospitals.

Constituency Involvement: NA

Objective 12:

Obtain and analyze data on inpatient hospital utilization by people with HIV infection.

Action Steps: Assemble and analyze database of hospital discharge data from all hospitals in 12 States.

Descriptions: Hospital Cost and Utilization Project.

Resources:

FY 95: $500,000

FY 96: $0

FY 97: $500,000

Populations Served: Patients with AIDS receiving inpatient care in hospitals in 12 states.

Constituency Involvement: NA

Objective 13:

To examine access to primary medical care for HIV positive African Americans who are linked to health services through community-based case management.

To improve access to primary medical care for HIV positive African Americans.

To create a model of assessment of primary health care access that could be utilized in other urban African-American communities.

Action Steps: In-depth structured interviews, unstructured interviews, focus groups, participant observation and direct observation.

Description: Study entitled "Access to Primary Health Care for HIV+ African Americans".

Agency for Health Care Policy and Research, continued

Resources:

FY 95: $21,600

FY 96: $0

FY 97: $0

Populations Served: African-American and Euro-American clients in the greater Tampa metropolitan area.

Constituency Involvement: New clients at three ethnically diverse community-based case management sites.

Objective 14:

To develop better conceptual and operational delineation of "health care related trust".

To describe the factors that potentiate or mitigate trust among HIV positive and HIV negative inmates.

To determine the effect of trust on health seeking behavior and adherence to medical therapy among HIV positive inmates.

Action Steps: In-depth interviews, focus group discussions, and administration of standardized surveys to inmates.

Description: Study entitled "Trust and HIV-Related Health Behavior Among Connecticut Inmates".

Resources:

FY 95: $21,600

FY 96: $0

FY 97: $0

Populations Served: Prisoners in Connecticut.

Constituency Involvement: HIV positive inmates in treatment, HIV positive inmates not in treatment, and HIV negative inmates.

Objective 15:

To gain an understanding of the health values and the determinants of health values of HIV positive patients.

Action Steps: Conduct focus groups, pose standard gamble, time tradeoff, and rating scale questions, and conduct intensive individual interviews.

Description: Study entitled "Understanding Health Values of HIV-infected Patients".

Resources:

FY 95: $0

FY 96: $160,160

FY 97: $0

Agency for Health Care Policy and Research, continued

Population Served: HIV-positive patients

Constituency Involvement: Patients will be recruited from a university-based AIDS treatment center which serves nearly all HIV positive patients in the study area.

Agency: Department and Health and Human Services, Food and Drug Administration

Goal 1: To ensure the safety and effectiveness of HIV-related therapeutic agents.

Objective:

Expedite access and approval of safe and effective drugs and biologics.

Action Steps: Encourage quality applications and data submissions to review division to ensure timely and efficient pre- and postmarket review.

Descriptions: Conduct meetings with sponsors to discuss drug development plans, expanded access programs, and accelerated approval options.

Facilitate scientific review of drugs and biologics by FDA advisory committees.

Resources:

FY 95: ~~$25,235,000~~ e 25.2 million
FY 96: ~~$25,235,000~~ e 25.2 million
FY 97: ~~$25,235,000~~ e 25.2 million

Populations Served: All persons who may benefit from approved therapeutic agents.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry and patient advocates.

Food and Drug Administration, continued

Goal 2: To ensure the safety and effectiveness of HIV-related preventive and therapeutic vaccines.

Objective:

Expedite regulatory review of promising products for preventive and therapeutic vaccines.

Action Steps: Expand partnership between FDA and its counterparts from outside organizations involved in vaccine development.

Descriptions: Encourage early consultation with sponsoring companies, develop guidance documents, exchange information, and work with other agencies and international organizations. Facilitate scientific review by FDA advisory committees.

Resources:

FY 95: ~~$11,863,000~~ 11.9 million
FY 96: ~~$11,863,000~~ 11.9 million
FY 97: ~~$11,863,000~~ 11.9 million

Populations Served: All persons who may benefit from approved preventive and therapeutic vaccines.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Goal 3: To ensure the effectiveness of test methodologies for HIV detection and measurement.

Objective:

Expedite improved test methodologies (such as diagnostic reagents and test kits) for HIV detection, confirmation, and viral load measurement.

Action Steps: Ensure timely and efficient pre- and post-market review.

Descriptions: Encourage early consultation with sponsor and develop guidance documents. Facilitate scientific review of drugs and biologics by FDA advisory committees.

Resources:

FY 95: ~~$8,732,000~~ 8.7 million
FY 96: ~~$8,732,000~~ 8.7 million
FY 97: ~~$8,732,000~~ 8.7 million

Food and Drug Administration, continued

Populations Served: All persons who may benefit from approved test methodologies for HIV detection and measurement.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Goal 4: To ensure the safety and effectiveness of HIV-related medical devices.

Objective:

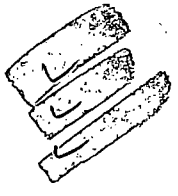
Expedited access and approval of safe and effective medical devices.

Action Steps: Encourage quality application and data submissions to ensure timely and efficient pre- and post-market review.

Descriptions: Conduct meetings with sponsors on study design; produce guidance documents. Facilitate scientific review of drugs and biologics by FDA advisory committees.

Resources:

FY 95: ~~$9,457,000~~ 9.5 million
FY 96: ~~$9,457,000~~ 9.5 million
FY 97: ~~$9,457,000~~ 9.5 million



Populations Served: All persons who may benefit from approved HIV-related medical devices.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

~~Food and Drug Administration, continued~~

Agency: Department of Health and Human Services, National Institutes of Health

Goal 1: To conduct and support natural history and epidemiological research to improve the understanding of the risk factors and mechanisms of HIV transmission and disease progression and to develop prevention strategies to reduce or prevent HIV transmission.

Objective 1:

Develop and assess intervention strategies to reduce or prevent HIV transmission in both domestic and international settings.

Action Steps: Develop and maintain the infrastructures to define populations in the United States and throughout the world with incidence and prevalence suitable for vaccine and other intervention trials (e.g. microbicides, barriers, treatment, behavioral) for preventing HIV transmission.

Support development and evaluation of improved, acceptable, effective physical and chemical barrier methods and conduct research on existing barrier methods to prevent sexual transmission of HIV and STDs.

Develop strategies and conduct studies to evaluate vaccines, drugs, and other interventions such as caesarian sections, vaginal cleansing, breast-feeding practices, nutritional interventions, and other approaches that prevent perinatal transmission.

Develop and assess the efficacy of strategies that may decrease transmission of HIV among drug users.

Develop and evaluate biological and behavioral interventions to control STDs as co-factors in HIV transmission.

Develop strategies that enhance safe sex behaviors and provide information on safe and effective contraceptive choices for at-risk women.

Develop methods to prevent infection in hard-to-reach gay male populations such as young, substance-using, and minority gay and bisexual men.

Develop methods of accessing hard-to-reach populations to identify factors that contribute to recruitment (and retention) into prevention and intervention activities.

Evaluate access to, acceptability of, and compliance with interventions such as AZT for perinatal transmission, condoms, and virucides.

Evaluate improved procedures for screening, monitoring, and inactivating HIV and other retroviruses in the blood supply; and develop and evaluate alternatives to blood transfusion.

Assess the impact of drug and alcohol abuse and mental health impairment on efficacy of behavior modification interventions directed at sexual transmission.

Develop effective drug treatment strategies for addiction, particularly focused on heroin and cocaine use.

National Institutes of Health, continued

Description: The development of biologically based interventions to interrupt transmission is an essential component of a comprehensive HIV prevention strategy that also includes behavioral intervention strategies as well as efforts to develop a vaccine(s). International studies should be supported with the goal of developing prevention strategies that can be used to reduce HIV transmission in the United States. Research is ongoing in these areas.

Epidemiologic studies, including vaccine preparedness research, provide opportunities for intervention research in defined cohorts of well-characterized populations. Strategies that employ therapies, devices, and other approaches, such as needle/syringe exchange programs using HIV seroconversion end points, are useful approaches for providing epidemiologic causation and evaluating effectiveness in preventing or reducing HIV transmission.

In addition, despite the fact that the blood supply in the United States is safer than it has ever been, it is important to develop even better methods for maintaining and improving its safety.

Objective 2:

Characterize the risk factors and mechanisms of HIV transmission in both domestic and international populations, with the goal of preventing transmission.

Action Steps: Evaluate HIV transmission in relationship to: viral factors such as virus load in the blood and at mucosal sites, characteristics of HIV (genotype and phenotype), and pre-existing infection with other agents; host factors such as contraceptives, pregnancy, menstrual cycle, substance abuse, and nutritional, immunologic and genetic determinants; local factors including intercurrent STDs, exogenous irritants, oral and anogenital inflammation, mucosal immunity, circumcision and cervical ectopy.

Further define the timing and mechanisms and risk factors in perinatal transmission, including breast-feeding.

Study mechanisms of resistance to HIV infection in persons who remain uninfected despite perinatal, sexual or parenteral exposure.

Define the determinants of high-risk behavior for transmission through drug use and sexual practices.

Characterize the dynamics of HIV transmission in epidemiologic studies of at-risk groups, including evaluation of sexual and drug-using networks, social and geographic mixing patterns, and turnover rates of at-risk populations.

Characterize the transmission and host immune responses of related retroviruses.

Description: Understanding the role of risk factors and mechanisms of HIV transmission is critical to the development of biologically and behaviorally based strategies to interrupt transmission of HIV. Epidemiologic studies provide important biological and behavioral information including the role of co-factors that may reduce or enhance transmissibility.

Objective 3:

Elucidate the progression of HIV infection, from its earliest stages through long-term sequelae, with the goal of understanding, preventing, and treating those factors.

Action Steps: Use epidemiologic studies to identify pathogenic mechanisms and co-factors for disease progression and disease-specific outcomes in well-defined subsets of individuals, individuals, including those with different rates of progression.

National Institutes of Health, continued

Conduct epidemiologic studies to understand the initiation and progression of early HIV infection, according to route of exposure, viral dose, viral genotype and phenotype, and host response, and how these early events influence disease progression.

Use epidemiologic studies to investigate the influence of viral genotype and phenotype on transmission efficacy and disease progression.

Use epidemiologic studies to evaluate the extent of dissemination of drug-resistant strains of HIV and its impact on pathogenesis.

Study the natural history of related retroviruses to elucidate retroviral pathogenesis.

Elucidate the mechanisms of HIV-associated carcinogenesis to improve strategies for early diagnosis and intervention.

Study HIV-infected children to determine: (1)mechanisms that contribute to impaired growth and neurodevelopment;(2)impact on childhood infectious diseases and the safety and efficacy of immunization;(3)impact on childhood psychosocial development, and (4)childhood-specific complications.

Evaluate the interaction of hormonal factors (including pregnancy, contraceptives, and hormonal replacement therapy) and HIV disease progression.

Study the progression of HIV-related disease in adolescents who have acquired their diseases as a result of drug use and/or sexual activity.

Study the natural history of HIV infection in the nervous system, including cognitive impairment, dementia, and neuropathy.

Describe the full spectrum of HIV-related diseases in HIV-infected populations.

Maintain and effectively utilize national specimen repositories for HIV-related studies.

Description: Epidemiologic studies provide a critical knowledge and resource base for more basic investigations of HIV pathogenesis. A better understanding of the diversity of HIV-related disease outcomes, co-factors for progression, and predictors of disease progression will be important in furthering attempts to develop HIV vaccines and more effective therapeutic interventions against HIV and its sequelae.

Objective 4:

Undertake epidemiologic research to reduce or prevent the occurrence of opportunistic illness in HIV-infected persons.

Action Steps: Study the impact of HIV infection on the emergence of new human pathogens and the impact of HIV infection on the reemergence of infectious diseases domestically and internationally.

Identify risk factors for the acquisition of opportunistic pathogens.

Study the determinants of the continuing occurrence of preventable opportunistic illnesses.

Study the role of transmissible and other preventable exposures in the etiology of AIDS-associated cancers and other outcomes.

Description: Most morbidity and mortality in HIV-infected persons result from the occurrence of opportunistic illnesses, including both infections and malignancies. Strategies to prevent these illnesses include prevention of exposure to the etiologic agents, prevention of disease in those who are exposed, and prevention of disease recurrence. Additional epidemiologic data are

National Institutes of Health, continued

needed to design more effective strategies to prevent the occurrence of these opportunistic illnesses.

Objective 5:

Develop and evaluate new laboratory assays, behavioral methods, and statistical techniques for epidemiologic studies.

Action Steps: Promote development and evaluation of virologic and immunologic assays to elucidate mechanisms of HIV transmission and disease.

Develop new survey and interview techniques to better measure HIV risk behaviors.

Develop new biostatistical techniques, including mathematical models, to better characterize transmission dynamics and disease progression.

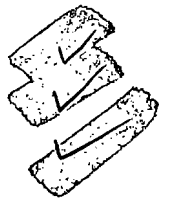
Develop innovative approaches for record linkages to study HIV-associated diseases and mortality.

Characterize the epidemiologic features of emerging HIV variants, including drug-resistant strains, diverse genotypes, and newly recognized geographic distribution.

Description: Epidemiologically defined populations contain well-characterized cohorts that can provide insights into HIV transmission, including resistance and susceptibility to infection and infectiousness, and into progression of HIV-related disease, from early infection through long-term sequelae, including cancer and neurocognitive impairment. The application of innovative biomedical research and behavioral strategies to such populations will greatly increase understanding at the biological level and will help to identify strategies for prevention of transmission and for clinical management of patients.

Resources:

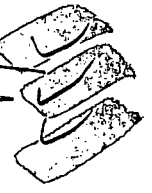
FY 95: ~~$192,624,000~~ 192.6 million
FY 96: ~~$205,812,000~~ 205.8 million
FY 97: ~~$203,285,000~~ 203.3 million



Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

~~***Unmet Needs:*** The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $33,986,000 over the FY 1997 figure.~~



National Institutes of Health, continued

Goal 2: To conduct and support research to improve the understanding of HIV and the pathogenic mechanisms of HIV disease.

Objective 1:

Delineate the cellular and molecular mechanisms associated with the viral immunopathogenesis of HIV-related immune dysfunction.

Action Steps: Delineate the direct and indirect mechanisms underlying HIV-induced depletion and dysfunction of target cells/tissues.

Define the virologic (load, phenotype, and genotype), immunologic (specific and nonspecific), pharmacologic, and environmental factors that contribute to disease progression and non-progression.

Delineate the mechanisms of virally triggered immunopathogenesis, including immune activation, induction of nonresponsiveness, and production of host factors, including cytokines, in pathogenesis.

Delineate the molecular mechanisms by which virus-encoded genes, gene products, and cellular factors regulate HIV replication and influence pathogenesis, with special emphasis on the use of primary virus isolates and cells.

Delineate the mechanisms of host genetic factors that mediate resistance or sensitivity to infection and influence disease progression.

Delineate the physiology and HIV-related pathophysiology of primary and secondary lymphoid organs, including hematopoietic precursor cells and their microenvironment.

Study the mechanisms of HIV infection that uniquely influence the developing immune system.

Further develop and utilize experimental models to examine the pathogenesis of lentiviral infections.

Establish and expand programs to facilitate access to and sharing of key patient samples, animal model resources, laboratory reagents, information databases, and quantitative virologic and immunologic assays.

Description: Basic scientific information regarding the cellular and molecular mechanisms that underlie HIV-related immune dysfunction and viral pathogenesis is critical to all areas of AIDS research.

Objective 2:

Delineate the molecular and cellular mechanisms of transmission and establishment of infection and their impact on disease progression.

Action Steps: Define the cellular and immune mechanisms that inhibit/enhance the early events in establishing HIV infection.

Determine the impact of early events in the establishment of HIV infection on the clinical course of the disease.

Determine the roles of specific and nonspecific mucosal and systemic immunity and other host factors that inhibit/enhance HIV transmission.

National Institutes of Health, continued

Determine the cell or tissue type that serves as the portal of entry of HIV and the impact of STDs and other pathogenic processes that influence HIV transmission.

Determine the role of viral phenotype/genotype and load on transmission of cell-free and cell-associated virus.

Elucidate unique aspects of HIV transmission and disease progression in under-researched populations.

Determine the mechanisms of vertical HIV transmission.

Description: The mechanisms of HIV transmission and the early events in the establishment of infection, and their relationship to disease progression, need to be better understood.

Objective 3:

Elucidate the etiologic factors and co-factors in the pathogenesis of AIDS-associated disease states. Enhance a bidirectional flow between basic and clinical observations and intervention programs ion HIV-related complications and foster interdisciplinary collaborations.

Description: Knowledge of AIDS-associated disease pathogenesis is urgently needed.

Sub-Objective 3a:

Elucidate the etiologic factors, co-factors, and mechanisms in the pathogenesis of HIV-related malignancies.

Description: Knowledge about the origins and pathogenesis of HIV-related cancers is urgently needed.

Action Steps: Elucidate the role of HIV infection, immune dysfunction, and interactions with potential co-factors in the development of HIV-associated malignancies.

Identify the characteristics of the host that predispose to development of malignant disease, including genetic, hormonal, and growth factors and immunologic characteristics.

Identify the pathogenic contributions of oncogenes, suppressor genes, carcinogens, and non-HIV viral and other microbial genes and proteins to HIV-associated malignancies; correlate these molecular factors with epidemiologic studies.

Establish and expand programs to facilitate development and sharing of *in vivo* animal models and patient specimens for HIV-associated malignancies.

Sub-objective 3b:

Elucidate the pathogenic mechanisms involved in HIV-associated neurological disease and neurobehavioral dysfunction.

Description: The damage that leads to both central and peripheral nervous system dysfunction must be better understood through studies of HIV-associated neuropathogenesis.

Action Steps: Investigate the characteristics of lentiviruses that invade the nervous system and the mechanisms by which these viruses cause nervous system impairment.

Study the effects of neurotrophins and immunoregulatory and proinflammatory cytokines on both host and viral gene expression.

Employ animal models of CNS-lentivirus infection that are crucial to understanding neu-

National Institutes of Health, continued

ropathophysiology.

Delineate the role of OIs and drug treatment in neurologic complications of AIDS, including CNS dysfunction and peripheral neuropathies.

Investigate biological and environmental factors that may affect nervous system function in the context of HIV-1 infection, emphasizing the role of psychoactive drug use.

Study mechanisms of HIV infection that uniquely influence the developing nervous system.

Develop technologies for correlative structural-functional analysis of progressive HIV-associated neurological and behavioral disorders and the progression of CNS disease.

Sub-objective 3c:

Elucidate the pathogenic mechanisms of HIV-related opportunistic infections.

Description: It is critical to understand the pathogenic mechanisms responsible for the development of HIV-associated OIs.

Actions Steps: Elucidate the mechanisms of immune function that mediate protection against OIs.

Study the effects of OIs on immune dysfunction and HIV disease progression.

Conduct studies of the basic biology and pathogenic mechanisms of opportunistic pathogens and their interactions with the host.

Develop *in vitro* techniques and animal models to propagate the opportunistic pathogens associated with HIV disease.

Develop and validate diagnostic assays for the reliable and rapid identification of HIV-associated OIs.

Identify biologic markers that are correlative for susceptibility and disease progression for HIV-associated OIs.

Identify and elucidate the genetic and environmental risk factors associated with susceptibility to and development and progression of OIs.

Sub-objective 3d:

Elucidate the etiology and pathogenesis of HIV-related disorders: gastrointestinal, renal, endocrine, cardiovascular, cutaneous, hematologic, oral, pulmonary, and other diseases.

Description: It is critical to understand various other organ/tissue-specific complications of HIV infection.

Action Steps: Investigate the etiologic and pathogenic mechanisms of HIV-associated gastrointestinal disease.

Identify the etiologic and pathogenic mechanisms of HIV-associated nephropathy.

Elucidate the etiology and pathogenesis of endocrine dysfunction and the role of alteration in the endocrine/immune axis in progression of HIV disease.

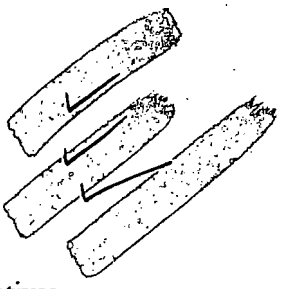
Elucidate the etiology and pathogenesis of HIV-related autoimmune disorders and cardiovascular, cutaneous, hematologic, oral, pulmonary, and other organ/tissue-specific disorders.

Indent to match sub-objectives on previous page

National Institutes of Health, continued

Resources:

FY 95: ~~$344,303,000~~ 344.3 million
FY 96: ~~$382,903,000~~ 382.9 million
FY 97: ~~$400,182,000~~ 400.2 million



Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Goal 3: To conduct and support preclinical and clinical research to develop, test, and optimize treatments for HIV infection, HIV-associated conditions, and for the prevention of HIV transmission.

Objective 1:

Improve understanding of the structure and function of molecular targets in order to develop improved assays for such targets; conduct screening, discovery, and preclinical development of novel anti-HIV agents and strategies (such as gene transfer technology and interruption of transmission) directed to the virus and/or host cell; and foster activity by and in collaboration with industry.

Description: Identify and develop novel anti-HIV therapies, particularly those therapies that impact at different stages of the life cycle of the virus.

Action Steps: Identify and characterize promising targets for anti-HIV therapy and extend knowledge of their mechanisms of action, develop relevant assays for identifying drugs active against those targets, and develop new compounds active at those targets, with emphasis placed on identifying agents active at novel targets other than reverse transcriptase inhibitors; emphasize agents that can effectively cross the blood-brain barrier.

Complete preclinical development, in cooperation with industry when appropriate, of promising new compounds and combinations of compounds and novel natural products, including assessment of toxicity, immunologic effects, pharmacokinetics, teratogenicity, and fertility in animal models and development of analytical method and chemical formulations.

Continue and accelerate domestic and international collection screening of large numbers of natural and synthesized compounds for anti-HIV activity, with a particular emphasis on the detection of agents that act at unique steps of the HIV life cycle with the intent of identifying lead compounds that can be modified for increased potency and other attributes (such as bioavailability and central nervous system penetration); develop and screen combinatorial libraries.

Emphasize basic and applied research to advance cross-NIH development of gene therapy; support development of preclinical laboratories to advance gene therapies; advance gene therapies, including new strategies for streamlining or eliminating ex vivo manipulation of

National Institutes of Health, continued

cells; develop more efficient and safe viral and non-viral gene delivery vectors; target tissue cells and subcellular compartments; develop effective antiviral genes; standardize evaluation of different gene therapies singly and in combination; and develop suitable lentivirus animal models for in vivo efficacy and safety studies.

Determine the high-resolution molecular structures for several of the HIV proteins and apply these structures to the rational design of drugs as part of the targeted drug development program; determine generalizable and effective approached for the use of macromolecular structure in designing drugs to combat HIV infection and AIDS; make resolved structures available in publicly accessible data bases.

Increase understanding of the mechanisms and limitations of drug resistance; study the effect of various agents on HIV replication and viral variation; evaluate early markers of resistance; evaluate the activity of anti-HIV drugs in various cell types (including macrophages) and in various stages of the cell cycle.

Develop new compounds capable of inhibiting the sexual transmission of HIV, such as topical microbicides (which may inhibit HIV and STDs associated with enhanced HIV transmission), HIV-specific viricides, and systemic agents.

Develop formulations that would be suitable for infants and children for both existing and experimental agents.

Evaluate transplacental passage of antiretroviral and other agents as well as the effects of these drugs on placental function and on the embryo/fetus in animal models.

Objective 2:

Conduct clinical trials and develop new trial methodologies for the treatment of HIV infection. Trials should be designed in order to rapidly develop new therapeutic strategies, optimize clinical efficacy and proper use of available modalities, define factors that affect the success of therapeutic strategies (including the role of resistance), and advance our understanding of disease pathogenesis and progression.

Description: Trials to evaluate new antiretroviral therapies alone and in combination will provide important information regarding resistance and synergistic effects of drugs that may eventually prolong the disease-free state and survival in HIV-infected individuals.

Action Steps: Support and improve clinical trials of potential therapeutic agents and combinations of agents in studies to determine pharmacokinetics and bioavailability and evaluate anti-HIV combinations that are non-cross-resistant, synergistic, and toxicity-sparing and that may delay development of drug-resistant HIV strains; enhance collaboration between and within ICDs to facilitate opportunities for clinical trials.

Implement the development and evaluation of virologic, immunologic, and clinical markers to assess drug activity and determine the prognostic value of surrogate markers in response to therapeutic interventions.

Support research and development of clinical trials methodology and study design so that appropriate pathways are taken rapidly to evaluate the activity, clinical efficacy, and ultimate acceptability of new agents and approaches that translate into clinical use.

Increase the understanding of the pathogenesis of HIV disease based on the evaluation of antiretroviral agents in clinical trials; establish effective mechanisms to evaluate therapeutic interventions and elucidate the pathogenesis of acute/early HIV infection.

National Institutes of Health, continued

Foster collaboration and better interactions with industry in drug development and evaluation efforts.

Evaluate safety, toxicity, and pharmacokinetics of retroviral agents provided to pregnant women, including transplacental passage of the agent, safety to the fetus/infant, and pharmacokinetics of drug elimination in the newborn. (Also noteworthy, assess the potential efficacy and feasibility of obstetric interventions to prevent vertical transmissions, such as cesarean deliveries and other aspects of intrapartum care.)

Enhance utilization of General Clinical Research Centers (GCRCs) for the conduct of single and multi-institutional clinical trials.

Develop and validate quality-of-life parameters included in patient assessments of clinical trials.

Support research on the effectiveness of pharmacologic (including compliance with therapies and STD prevention) and non-pharmacologic including psychosocial) interventions (including nutritional factors and adherence improvement).

Investigate possible interactions between therapies for HIV-related disease and other substances that HIV-infected individuals might use, such as drug-abuse treatment medications, oral contraceptives or other prescription drugs, nonprescription drugs, alternative or complementary therapies, or drugs of abuse.

Coordinate studies to encourage co-enrollment of patients on all trials where appropriate (co-enrollment would not only allow for better utilization of limited resources but also enable assessment of concomitant medications and their interactions, improving the efficiency of the primary study).

Develop a coordinated plan to evaluate long-term therapeutic strategies, e.g., develop plans for long-term follow-up, enroll patients in sequential randomized trials once they have reached an end point in their initial trial.

Support clinical trials to evaluate the safety and pharmacokinetics of existing and experimental agents for use in treating HIV-infected infants and children; evaluate the effects of puberty on the pharmacokinetics of antiretroviral agents and other drugs for the treatment/prophylaxis of HIV infection and the pharmacokinetics of drugs in adolescents.

Evaluate potential late toxic effects of antiretroviral therapy given to infants and children.

Objective 3:

Develop and evaluate strategies that will enhance, restore, and/or maintain the immune systems of HIV-infected individuals and extend our understanding of immunopathogenesis.

Description: Essential to HIV research efforts are studies directed toward finding therapies that can restore, enhance, or maintain the integrity of the immune system.

Action Steps: Evaluate therapeutic approaches that test specific hypotheses of HIV immunopathogenesis,

Develop and validate new methods for evaluating immune function in the context of clinical trials.

Continue and accelerate the testing of cytokines, modulators of cytokines, and other immunomodulating agents either singly or in combination with antiretroviral agents for the purpose of reconstituting the deficient immune systems of HIV-infected individuals.

Develop and evaluate various approaches of active and passive immunotherapy for both HIV

National Institutes of Health, continued

infection and its sequelae.

Develop a program of reconstituting the immune systems of HIV-infected individuals by administration of cellular elements in an autologous, syngeneic, or allogeneic fashion, including use of expanded peripheral blood T cells, bone marrow transplantation, thymic transplantation, cord blood, stem cells, and/or xenogeneic transplantation.

Develop new therapeutic strategies based on gene therapy approaches to protect hematopoietic stem cells and thereby reconstitute the immune system with HIV-resistant lymphoid, monocytic and other cellular compartments.

Use structural biologic techniques to determine the structures of various cytokines and cytokine receptors as potential targets for HIV therapies.

Increase collaboration of ICDs by joint funding of projects to facilitate the conduct of immune-based therapeutic trials and to enhance pathogenesis-related research in HIV-infected individuals.

Foster collaboration and better interactions with industry in developing and evaluating immunorestorative/immune-enhancing agents.

Define the mechanisms of immunomodulating agents and proceed with preclinical studies of the most promising agents.

Objective 4:

Discover, develop, and evaluate potential agents for prevention and treatment of HIV-associated OIS and other infections modified by HIV infection.

Description: Opportunistic infections (OIs) are the most common cause of morbidity and mortality in HIV-infected individuals. Continuing to develop and evaluate therapies for preventing and treating OIs is essential for decreasing morbidity and improving survival.

Action Steps: Support basic research on OIs in order to increase fundamental knowledge and to identify new therapeutic targets and strategies and understand how pathogens contribute to morbidity. Determine the high resolution molecular structures for OI proteins and apply these structures to the rational design of drugs as part of the targeted drug development program and determine generalizable and effective approaches for the use of macromolecular structure in designing drugs to combat OIs associated with AIDS.

Support discovery and preclinical programs to develop therapies especially targeting cryptosporidia, microsporidia, JC virus, HPV, and azole-resistant fungal organisms, with emphasis on bioavailable agents with favorable pharmacokinetics. Develop *in vitro* culture systems for OIs such as *Pneumocystis carinii* (PCP).

Further conduct clinical trials for the prophylaxis and treatment of HIV-associated OIs in HIV-infected individuals. Important OIs include *Mycobacterium tuberculosis* infection (TB), *Mycobacterium avium* complex, cytomegalovirus infection, cryptosporidiosis, microsporidiosis, cryptococcal disease, azole-resistant fungal infection, toxoplasmosis, PCP, acyclovir-resistant herpes infections, progressive multifocal leukoencephalopathy (PML), bacterial infections, and other infections whose course is affected by HIV. Evaluate immune-based therapies as adjuncts for treating OIs.

Determine the optimal strategies and combinations of agents to prevent and treat multiple OIs (by simultaneous prophylaxis of multiple opportunistic pathogens) and determine their effects in combination with antiretroviral agents. Strategies need to focus on the subgroups at

National Institutes of Health, continued

increased risk, time of initiation, compliance, pharmacologic interactions, toxicities and adverse reactions (e.g. trimethoprim sulfamethoxazole reactions), and minimizing development of resistance; studies should include quality-of-life assessments and cost-benefit analyses.

Develop and utilize animal models for preclinical efficacy, pharmacokinetics, and safety testing of potential agents for OIs, including mutagenicity and teratogenicity.

Develop clinically useful assays for the rapid diagnosis of disease, treatment response, and sensitivity testing of OIs, especially TB, MAI, enterics, and infections produced by CMV, fungi, Toxoplasma, and JC virus, including use of specimens in existing repositories.

Determine the role and capability of preexisting immunity (both induced and natural) to control OIs and the ability of HIV-infected individuals to respond to vaccination throughout the course of infection and disease; assess possible interaction of vaccination and HIV replication.

Explore the bidirectional interactions between OIs and HIV infection including possible impact of opportunistic pathogens on the clinical expression and acceleration of HIV disease and vice versa.

Support clinical trials to evaluate the safety and pharmacokinetics of existing and experimental agents for use in preventing and treating OIs in HIV-infected infants, children, and pregnant women.

Objective 5:

Develop, evaluate, and implement strategies for interrupting vertical transmission of HIV from mother to child and extend out understanding of perinatal transmission and the pathogenesis of early infection (treatment of children will be addressed in other objectives).

Description: Vertical transmission of HIV from mother to child is the predominant mode of transmission for pediatric HIV infection. The identification, development, and testing of interventions should be based on the pathogenesis of transmission.

Action Steps: Support the rapid translation of basic research observations to strategies for the interruption of vertical transmission; apply the results of clinical trials to the investigation of pathogenesis and to clinical practice.

Support national and international collaborative studies to retrospectively and prospectively evaluate potential obstetric factors associated with vertical transmission including non-protocol use of antiretroviral agents.

Develop and evaluate strategies for interrupting the vertical transmission of HIV from pregnant women to their offspring that are simpler and less costly than the current AZT regimen and derive information on pathogenesis of transmission from the study of these strategies. Such strategies include antiviral agents, anti-HIV immunoglobulin, monclonal antibodies, vitamin supplementation (e.g. vitamin A), HIV vaccines, adjuvants, virucides, and other intrapartum interventions alone and in combination.

Evaluate the safety, toxicity, pharmacokinetics, and antiretroviral activity of anti-HIV agents in pregnant women and newborns; explore the use of highly active agents that may develop resistance rapidly and could be used in this setting.

Assess the potential efficacy and feasibility of obstetric interventions to prevent vertical transmissions, such as cesarean deliveries and other aspects of intrapartum care.

Develop and improve sensitive and specific diagnostic parameters that are accessible and cost-effective to permit early differentiation of HIV infection status in children born to

National Institutes of Health, continued

HIV-infected mothers.

Investigate the role of the placenta in transmission of anti-HIV drugs from mother to fetus.

Expand the obstetrical and pediatric infrastructure for the conduct of perinatal trials through collaborative efforts, particularly in the international setting.

Support the long-term follow-up of women and children who participate in perinatal trials to evaluate potential distant effects of antiretroviral agents and/or biologics.

Evaluate the risk of vertical transmission of drug-resistant virus.

Evaluate incorporation of ACTG 076 AZT regimen into clinical practice in the United States.

Evaluate therapeutic strategies for treating infants during acquisition of HIV to determine whether disease progression can be significantly altered.

Objective 6:

Discover, develop, and evaluate improved strategies for the treatment and prevention of HIV-associated malignancies and extend our understanding of the risk factors for and pathogenesis of such malignancies.

Description: HIV-associated malignancies have a significant impact on morbidity and mortality, and some are expected to become increasingly common as survival with sever immune dysfunction is prolonged and as the demographics of HIV infection change. The development of methods to identify persons at high risk for subsequent malignancy, and the identification, development, and clinical testing of new therapeutic strategies for these malignancies are essential.

Action Steps: Support basic research on HIV-associated malignancies to increase fundamental knowledge of the etiology, pathogenesis, and biology of these neoplasms; develop preclinical models for testing potential therapeutic strategies.

Identify novel mechanisms and targets (e.g. cytokines, angiogenesis, viral or hormonal co-factors) for treatment and prevention of HIV-associated tumors, including Kaposi's sarcoma (KS), non-Hodgkin's lymphoma, HPV-associated malignancies, and others, and develop new therapeutic strategies on the basis of these findings.

Use structural biologic and biochemical information to rationally design drugs to inhibit specific pathogenic factors of HIV-associated malignancies.

Develop *in vivo* models (SCID/nude mouse) for pathogenesis and drug sensitivity testing.

Develop *in vitro* models of KS as well as assays for angiogenesis inhibitors.

Encourage the develop and coordinate the conduct of clinical trials that concurrently evaluate antiretroviral and anti-OI therapeutic strategies directed against the malignancy in order to assess the effects of such treatment on the malignancy as well as on the underlying HIV infection, immune function, and clinical course.

Continue and expand screening, discovery and development of novel therapeutic agents with activity against HIV-associated malignancies (e.g. agents with better CNS penetration, agents with better safety profiles).

Develop trials to optimize existing therapies for malignancies in HIV-infected patients, including therapeutic adjuncts such as hematopoietic colony-stimulating factors and supportive care; develop and validate quality-of-life assessments.

National Institutes of Health, continued

Encourage collaborative studies to develop mechanisms for early identification of patients at high risk for malignancy and to develop and assess interventional strategies to reduce or prevent the development of malignancies.

Improve diagnostic methods for early diagnosis of malignancies and for early detection of recurrent cancer.

Improve collaboration between various adult and pediatric cooperative groups conducting clinical trials of HIV-associated malignancies and ICDs and industry to accelerate trials completion and approval of active agents.

Foster prompt referral of patients (co-registration) from antiretroviral trials to trials for AIDS-related malignancies.

Objective 7:

Develop strategies for assessing,preventing, and treating central and peripheral nervous system dysfunction in the course of HIV infection.

Description: Nervous system impairment, including AIDS-related cognitive/motor dysfunction (formerly AIDS dementia complex), and peripheral nerve/spinal cord dysfunction are serious sequelae of HIV disease.

Action Steps: Develop novel strategies and agents that are active against putative pathways of HIV-induced CNS dysfunction, e.g inhibitors of quinolinic acid, excitatory neurotransmitters, gp160/120, and other potential neurotoxins.

Implement studies related to the delineation of mechanisms responsible for impaired neurocognitive development in children born to HIV-infected mothers, and develop strategies directed at the prevention and treatment of this complication of HIV infection; utilize insights from the impaired state to better understand the course of normal neurocognitive development.

Implement clinical trials addressing nervous system complications of HIV infection and incorporate neurologic and neuropsychological assessments into other HIV-related clinical trials.

Develop therapeutic agents and/or delivery systems that are capable of crossing the blood-brain barrier and develop carriers that capitalize on different mechanisms to deliver drug to the CNS and are active against HIV infection; assess the safety of these different preparations; develop an understanding of physical and physiological mechanisms involved in penetration of the blood-brain barrier, and possibly develop agents that could conceivably block HIV entry into the CNS.

Better delineate etiologies of peripheral neuropathy in HIV infection, and develop strategies to prevent and treat this complication.

Develop and utilize *in vitro* and animal models of CNS impairment and AIDS-related cognitive/motor dysfunction to further identify agents that can reverse HIV neuropathogenesis.

Implement assessments and approaches for the diagnosis of HIV-related dementia in clinical studies; improve implementation of standardized adult, adolescent, and pediatric neuropsychologic and neurologic assessment batteries in clinical studies and evaluate treatment-induced changes in neurocognitive impairment in a linguistically and culturally sensitive context.

Develop alternative methods for detecting and assessing response to treatment of central and peripheral nervous system dysfunction including brain structural, spectroscopic, and functional imaging (for dementia); develop quantitative summary testing and examination of cutaneous nerve fibers in neuropathy.

National Institutes of Health, continued

Objective 8:

Develop and evaluate therapies for the treatment and prevention of serious HIV-associated complications, especially wasting syndrome and growth failure, as well as other disorders including hematologic, dermatologic, renal, metabolic, pulmonary, and oral manifestations.

Description: Important clinical sequelae of HIV infection include wasting syndrome, growth failure, metabolic disorders, dermatologic disorders, ITP, nephropathy, oral diseases, and other symptoms and serious complications. Drugs and strategies that can treat these sequelae are needed to ameliorate these conditions.

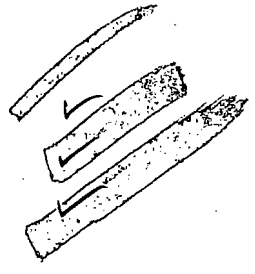
Action Steps: Develop and evaluate therapeutic strategies for preventing and ameliorating the various sequelae of HIV infection (listed above in the Description) and increasing understanding of their pathogenesis.

Develop and validate quality-of-life parameters for adults and children for the various sequelae of HIV infection (listed above in the Description).

Develop and evaluate therapeutic strategies for alleviating the various symptoms of unclear etiology in HIV-infected persons (listed above in the Description) and improving the quality of life.

Resources:

FY 95: ~~$462,929,000~~ 463 million
FY 96: ~~$472,944,000~~ 473 million
FY 97: ~~$470,042,000~~ 470 million



Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Goal 4: To conduct and support basic, preclinical, and clinical research to develop a safe and effective preventive HIV vaccine.

Objective 1:

Increase scientific knowledge of host defense mechanisms leading to protection against HIV infection and disease.

Description: More basic knowledge is needed to define protective immune responses to HIV in order to facilitate the development of vaccines and other immunologic strategies to prevent and control HIV infection.

Action Steps: Develop animal models that are practical and as much as possible are representative of the spectrum of HIV infections and AIDS; models should be amenable to use in

National Institutes of Health, continued

evaluating protection by vaccines and, where this can be demonstrated, determining the correlates of protective immunity.

Determine the mechanisms of immunologically mediated control of infection with HIV and other related retroviruses, including the role of specific and nonspecific immunity in inhibiting viral replication.

Additional basic knowledge is needed to determine:

- factors, including persistence of antigens, that favor establishment of memory and development of long-term protective immunity;
- the heterogeneity of specific responses to an immunogen within distinct compartments of the immune system;
- factors that promote development of particular effector cell types;
- mechanisms resulting from exposure to HIV that interfere with induction or propagation of vaccine-induced effector responses;
- mechanisms of virus neutralization.

Study acutely infected individuals, exposed/uninfected humans (and other primates), and rapid/nonprogressors to determine viral and host factors that impact amounts of circulating virus and disease course; ensure that plasma, PBMC, biopsy, autopsy, and other key patient and animal samples, including CNS samples, are accessible to qualified laboratories.

Define and characterize viral B cell and T cell epitopes that induce protective immunity; understand their structure and antigenicity and determine whether and how their immunogenicity can be exploited in vaccine development; and define epitopes in which substitutions cannot be tolerated by the virus.

Determine whether infection with one strain of HIV or related retroviruses confers protection against subsequent infection with a second strain; determine the protective mechanism and timing.

Understand how and why HIV and related lentiviruses evade or escape from humoral and cellular arms of the immune response.

Explore strategies to elucidate the obligate mechanisms for protective immunity against HIV, including amplification of selected responses by passive transfer of Ab or immune cells and subtraction by deletion of selected components of the immune system.

Study chronic infection with attenuated viruses, such as SIV variants shown to induce strong protection against virulent SIV strains in macaques, to understand what properties of the virus and the immune system are responsible for lack of disease induction and protection from challenge with wild-type virus.

Explore the molecular epidemiology and serology of HIV-1 populations relevant to vaccine trials and collect clinical material from these populations for scientific analysis. Acquire epidemiological information to assist in interpretation of these analyses.

Develop quantitative measures of HIV concentration in bodily fluids to determine whether there is a relationship between HIV concentration and transmission and to determine the effect of concurrent STDs on HIV shedding.

Objective 2:

(Bring up (ext) ↑

National Institutes of Health, continued

Apply findings from basic, epidemiologic, and clinical research to the design and evaluation of vaccine strategies in laboratory studies and animal models, and foster collaboration with industry in the research and development of candidate vaccines.

Description: The identification of viral antigens and vaccine delivery methods that elicit long-lasting protective immune responses against a broad range of HIV isolates will facilitate development of effective vaccines.

Action Steps: Support the design and development of potential vaccines, including vaccines composed of:

- whole-killed HIV and genetically engineered, noninfectious HIV mutants that lack the viral RNA genome or have a defect in a critical gene necessary for replication but contain an array of HIV genes for expression of antigenic proteins;
- live, recombinant viral and bacterial vectors engineered to express one or more HIV proteins;
- naturally occurring and genetically engineered, live-attenuated strains of HIV;
- synthetic peptide candidates capable of inducing and boosting both cellular and humoral immunity;
- DNA coding for viral proteins;
- agents that stimulate mucosal immune responses;
- a combination of the above agents and preparations;
- other novel agents and preparations.

Evaluate the efficacy of vaccine strategies in animal models of HIV and related lentiviruses.

To accomplish this:

- test vaccine strategies in animal models that most closely mimic the HIV infection in humans;
- determine the effect of vaccine formulation and regimen as well as the nature, timing, and route of vaccine challenge on the characteristics and effectiveness of the vaccine-induced immune response;
- define the impact of different vaccine approaches on kinetics of immune responses, kinetics and localization of viral replication, disease progression, and biologic characteristics of breakthrough virus including transmissibility;
- conduct long-term follow-up of vaccinated animals that become chronically infected to determine the impact of vaccination on disease progression;
- develop assays to distinguish between infection and serological responses due to immunization.

Support design and development of methods to improve or modulate immune responses (qualitatively or quantitatively), including:

- novel adjuvants and presentation methods;
- vaccines incorporating cytokines or other biologically active molecules;
- establishment of physical or biological reservoirs for long-term antigen presentation;
- other novel strategies.

National Institutes of Health, continued

Encourage development of candidate vaccines of suitable antigenic types and possessing stability and route of administration

characteristics appropriate for international as well as domestic use.

Characterize and evaluate the potential negative side effects of candidate vaccines, including production antibodies enhancing neurotoxicity and oncogenicity.

Develop better *in vitro* methodologies to measure immune responses to primary viral isolates.

Develop infrastructure, and address scientific, legal, and regulatory issues to foster and encourage participation by, and collaboration with, industry and other agencies in the research, development, production, and clinical testing of candidate vaccines.

Objective 3:

Select candidate vaccines or concepts suitable for Phase I and Phase II trials and conduct these trials.

Description: Suitable candidate vaccines need to be selected and evaluated in Phase I and Phase II trials to determine safety and immunogenicity.

Action Steps: Support the conduct of Phase I and Phase II coordinated clinical trial that will determine long-term and short-term safety and compare immunologic responses to preventive vaccine candidates; include a broad range of humoral, cell-mediated, and mucosal immune parameters;

Develop a mechanism to evaluate the suitability of vaccine candidates for entry into Phase I and Phase II trials; evaluation criteria should include originality and intrinsic value of the concept and animal model data.

Develop strategies at the local and national levels to reduce social and economic risk to volunteers in Phase I and Phase II trials to facilitate broad participation.

Design and conduct Phase II trials using promising HIV vaccines that are also genetically or immunologically related to HIV isolates circulating in the proposed trial population and of an appropriate size to facilitate decisions regarding efficacy trials. Analyze immune responses in vaccines and appropriate controls. Isolate and characterize virus and follow clinical course and immune responses of vaccines who become HIV-infected.

Study viral isolates from participants in HIV vaccine trials and selected controls to explore the possible effects of vaccination on the characteristics of transmitted viruses.

Conduct behavioral research on trial participants to establish whether their risk behavior has been influenced by participation in a vaccine trial, with emphasis on individuals who become infected while participating.

Closely coordinate the evaluation of research findings on prophylactic AIDS vaccines with preclinical research and immunotherapeutic interventions.

Objective 4:

Identify mechanisms of protective immunity to HIV in newborns and infants and support the development of safe and effective immunologic strategies for preventing or controlling HIV infection in this population.

Description: Distinct approaches and infrastructure are needed to achieve protection of

National Institutes of Health, continued

newborns and infants because of the unique nature of their immune responses and modes of exposure to HIV.

Action Steps: Determine what viral, immunologic, and non-immunologic host factors influence transmission of HIV-1 from mother to infant;

- Compare virus isolates that are and are not transmitted from mother to infant;
- Seek maternal and infant immune responses that might prevent transmission to infants.

Develop and maintain domestic and international infrastructure necessary to enroll mothers and infants in prospective long-term follow-up vaccine trials and other interventions.

Determine the safety and immunogenicity of various HIV vaccines and adjuvants in relevant animal models of maternal-fetal and maternal-infant transmission to evaluate safety, immunogenicity, and efficacy of candidate vaccines.

Select and evaluate antibody and/or cellular preparations in passive or passive/active HIV prevention studies.

Establish criteria for advancement of candidates in Phase I, Phase II, and Phase III clinical trials in children.

Conduct Phase I, Phase II, and Phase III clinical trials in children for the most promising candidates that meet established criteria.

Objective 5:

Identify appropriate domestic and international population and develop infrastructure and collaborations with government, communities, and industry necessary for ensuring adequate performance of Phase III efficacy trials.

Description: Preparation for HIV vaccine efficacy trials requires development of an infrastructure and a series of studies and planning activities to ensure their feasibility.

Action Steps: Develop domestic and international sites with access to populations at high risk for acquiring HIV infection, where vaccine or other prevention research activities may be feasible.

Establish linkages with communities or community organizations where efficacy trials might be conducted to optimize education, recruitment, and follow-up activities and to help address community concerns related to AIDS vaccine efficacy trials.

For international trials, work closely with national (host) governmental and regulatory authorities, collaborating institutions, vaccine manufacturer(s), and the World Health Organization to plan and conduct vaccine efficacy trials adhering to the highest ethical and scientific standards.

Carry out appropriate epidemiologic studies that determine the risk profiles and infection rates of various populations in the United States and worldwide in order to identify those groups most likely to be the participants in vaccine trials.

Maintain the necessary laboratory infrastructure at designated sites for conducting domestic and international vaccine efficacy trials.

Acquire and analyze HIV isolates from recent seroconverters representative of potential efficacy trial populations so that genetic and antigenic information about virus circulating in the population can be obtained.

Evaluate other biomedical and behavioral interventions that could prove of benefit in

National Institutes of Health, continued

decreasing the incidence of HIV infection in the populations identified for future vaccine efficacy trials and assess their potential impact on the evaluation of vaccine efficacy.

Conduct behavioral research in populations at high risk for HIV infection to determine, for example, appropriate risk-reduction interventions and to estimate risk behavior and recruitment, adherence, and retention strategies pertinent to the design and execution of a successful efficacy trial, especially for populations that have been historically underrepresented in clinical trials.

Determine possible adverse social, economic, or legal consequences of participation in clinical trials, and develop strategies for mitigating potential harm.

Determine optimal methods of achieving informed consent for vaccine efficacy trials.

Prepare for adequate long-term follow-up of individuals participating in vaccine clinical trials where it will be necessary to determine the longevity of immune response, the correlates of immune protection, long-term safety, the impact of participation on risk-taking behavior, and the possible positive or negative effects of vaccine immunization against disease progression and HIV transmission.

Encourage linkage between vaccine preparedness studies in high-risk populations and other research activities including research on TB and STDs; and integrate research on vaccines against opportunistic infections as appropriate.

Objective 6:

Select suitable vaccine candidates and support efficacy trials when appropriate criteria are met.

Description: Conduct HIV vaccine efficacy trials of the most promising candidate vaccines in well-characterized, high-risk populations to identify effective vaccines for the control of HIV infection.

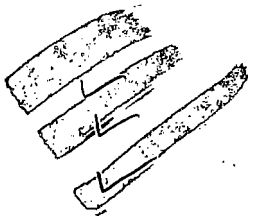
Action Steps: Establish criteria with concurrence of an advisory group that has the requisite scientific, public health, government and community expertise.

Conduct large-scale efficacy trials of preventive vaccine candidates that have proven promising, safe, and immunogenic in Phase II trials and that meet appropriate criteria;

- Evaluate HIV vaccine candidate efficacy against infection and disease;
- Evaluate additional virologic, immunologic, and behavioral outcomes, particularly correlates of protective immunity.
- Ensure that trials are conducted with the highest regard for social and ethical standards.

Resources:

FY 95: ~~$100,399,000 e~~ 100.4 million
FY 96: ~~$109,533,000 e~~ 109.5 million
FY 97: ~~$116,132,000 e~~ 116.1 million



Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

National Institutes of Health, continued

Goal 5: To conduct and support behavioral and social science research to further understanding of the determinants and processes that influence behaviors associated with HIV transmission and to develop and improve HIV prevention intervention strategies.

Objective 1:

Support research to develop and evaluate social and behavioral interventions at the societal, community, organizational, and individual levels to reduce HIV transmission by reducing HIV-related risk behaviors and increasing protective behaviors. Multi-site and cross-national studies are encouraged.

Description: Studies have demonstrated that HIV-related risk behaviors can be measured and modified. In response to the evolving epidemic, an expanded HIV prevention research agenda is called for on what works, for whom, where, for how long, and at what cost.

Action Steps: Develop and evaluate the effectiveness and cost-effectiveness of demographically and culturally appropriate behavioral and social interventions in different domestic and international settings and populations to reduce high-risk HIV-related behaviors and HIV transmission (e.g. through safer sexual practices, increased use of condoms and other barrier methods, use of sterile injection equipment, and reduction of high-risk drug-related behaviors).

Support research on a range of HIV prevention strategies in a variety of settings for both emerging populations and groups that continue to be at high risk for HIV.

Support research to increase the effectiveness and cost-effectiveness of drug abuse, mental health, and alcoholism treatment, including the development of new pharmacotherapies, to reduce HIV-related risk behavior in different settings and populations.

Support research (including multi-site and cross national studies) on comprehensive interventions that integrate various HIV and STD prevention and family planning approaches.

Support research to improve the access to, delivery of, evaluation, and cost-effectiveness of services that reduce HIV risk behaviors and transmission.

Design and test interventions to increase recruitment, retention, and adherence to protocols for HIV prevention research, including prophylactic vaccines.

Support research to improve the transfer of effective interventions to and from community planning processes.

Objective 2:

Support basic research to strengthen the understanding of determinants and processes that influence HIV-related risk behaviors and the consequences of HIV disease.

Description: Understanding the basic factors influencing behavior and behavior change at the societal, community, organizational, and individual levels is necessary for the development of interventions to prevent the transmission of HIV and to ameliorate its adverse consequences. Research is needed to define the behavioral, psychological, cognitive, and social consequences of HIV infection, disease progression, and treatment.

National Institutes of Health, continued

Action Steps: Develop models of behavior and behavior change that integrate biological, psychological , and social perspectives to explain and predict the acquisition, change, and maintenance of HIV-related behaviors among individuals and groups in various settings.

Study the social, structural, and cultural factors such as class, ethnicity, sexual identification, age, and gender that influence HIS-related behavior, affect access and delivery of care, and determine intervention strategies.

Study the development and maintenance of HIV-related risk and preventive behaviors in specific social contexts such as the sexual dyad, peer groups, social and drug-using networks, families, and communities.

Conduct research on decision-making processes, which may include disclosure of one's HIV-status, choice of treatment options, and adoption of protective behaviors.

Support research to understand the processes of how communities become involved in HIV intervention research.

Identify the behavioral, psychological, cognitive, and social consequences of HIV disease for HIV-seropositive individuals, their support systems (e.g. partners, family members, and other care givers), and their communities.

Support studies in animal models in behavior and behavior change relevant to HIV infection and prevention.

Conduct research that identifies the social and behavioral factors affecting recruitment, retention, and adherence in clinical trials.

Conduct research on the barriers to preventive actions based on lack of trust and misinterpretations of meaning of information related to HIV.

Objective 3:

Support research for the discovery, development, and evaluation of strategies for preventing or minimizing the negative physical, psychological, cognitive, and social consequences of HIV, including stigmatization of persons with or at-risk for HIV infection. Support research strategies for promoting effective health care utilization among persons with HIV infection.

Description: Enhancement of the quality of life of seropositive individuals and facilitation of HIV treatment require further research on interventions to affect the physical, behavioral, psychological, cognitive, and social consequences of HIV infection, disease progression, and treatment. Research is also needed to improve delivery of care to diverse population groups.

Action Steps: Develop and evaluate interventions for promoting quality of life and to delay or prevent physical, behavioral, psychological, cognitive, and social consequences.

Promote research to identify and remove barriers to effective health care utilization among persons with or at-risk of HIV infection, including access, engagement, follow-up, and adherence to health and social services across the care continuum (e.g. testing and counseling, health care-seeking behavior, adherence, case management, and home/hospice care). This strategy may entail developing and testing innovative models of treatment delivery for HIV disease at all illness stages.

Develop and evaluate interventions for promoting increased recruitment, adherence, and retention, especially in underrepresented populations, in HIV treatment and clinical trials.

Test models of care-giving for people living with HIV disease, their significant others,

National Institutes of Health, continued

extended family members, and care providers.

Develop and evaluate interventions for preventing social stigmatization of persons with or at-risk of HIV infection and AIDS in different settings (e.g. workplaces, schools, health care facilities, and prisons).

Objective 4:

Support research to advance innovative quantitative and qualitative methodologies to enhance HIV behavioral and social science research.

Description: Behavioral and social science methods have greatly advanced our understanding of HIV transmission and health maintenance. Further refinement of established methods and rapid development of emerging technologies are essential to continued improvement of our knowledge of HIV-related behaviors; our understanding of linkages between HIV-related risk behaviors, transmission, and disease progression; and the evaluation of interventions.

Action Steps: Develop improved qualitative and quantitative methodologies for studying behavioral and social factors associated with HIV, including improved methods for validating self-report data, improved measurement tools for surveys, and the measurement of change over time.

Develop improved sampling strategies for sub-populations and culturally and linguistically sensitive and appropriate research instruments.

Develop improved methods and techniques for dealing with subject attrition and missing data.

Encourage secondary data analysis by developing techniques to protect confidentiality and by using of meta-analysis.

Develop and refine techniques for measuring social networks associated with HIV.

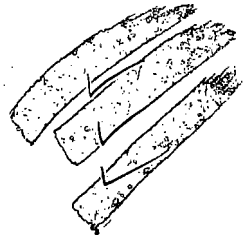
Develop and refine research techniques for measuring responses by organizations to HIV and for characterizing organizations working in the HIV field.

Encourage studies that will support multi-site studies and cross-national comparisons.

Develop and refine mathematical models for linking behavior change interventions with reduction in HIV transmission.

Resources:

FY 95: ~~$170,984,000~~ e 171 million
FY 96: ~~$174,077,000~~ e 174 million
FY 97: ~~$180,238,000~~ e 180 million



Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Goal 6: To provide appropriate training and infrastructure for the conduct of HIV-related biomedical and behavioral research domestically and internationally.

Objective 1:

Provide both domestic and international training in biomedical and behavioral research on HIV.

Description: Meeting the needs of research on HIV/AIDS requires recruiting and training basic, clinical, and behavioral scientists in the United States and abroad in the many disciplines necessary to carry out this diverse scientific agenda.

Action Steps: Maintain pre-doctoral and post-doctoral training, as well as advanced research training, in a range of AIDS-related disciplines.

Sponsor an annual AIDS Fellows Meeting to promote collaboration and information dissemination.

Support training of scientists and clinical investigators in basic AIDS research to better link basic and clinical pathogenesis research.

Stimulate pre-doctoral and post-doctoral training in prevention, behavior change, and adherence and compliance to treatment.

Promote training of biomedical and behavioral scientists in the use of high-performance computing systems for HIV-related research.

Support training and research capacity to deal with the epidemic of tuberculosis (TB), including multiple drug resistance associated with HIV infection.

Maintain participation in the Fogarty International Center (FIC)-sponsored international training and research programs and expand these programs by recruiting trainees from additional countries in Asia and Latin America, with the long-term goal of providing AIDS-related training for leading health scientists from all developing countries.

Explore new grant mechanisms to link U.S. AIDS research scientists and institutions with leading AIDS research scientists and institutions in foreign countries.

Support both pre-doctoral and post-doctoral training in structural biology.

Support the NIH AIDS Loan Repayment Program to bring scientists and physicians to the NIH to expand the cadre of trained intramural researchers.

Support both pre- and post-doctoral domestic and international AIDS-related training in epidemiology, biostatistics, and behavioral methodologies.

Establish appropriate career training programs for laboratory investigators, clinical investigators, and translational scientists (i.e. making the transition from bench to patient).

Support training of investigators in applied immunobiology.

Support training of basic investigators, clinical investigators, and translational investigators for OI research.

Support training of basic investigators, clinical investigators, and translational scientists for research on malignancies in HIV-infected patients.

Collaborate with other PHS agencies in the development of training regarding HIV preven-

National Institutes of Health, continued

tion, treatment, research, and education for health care providers, AIDS service providers, and health educators.

Objective 2:

Establish appropriate infrastructure for the conduct of HIV research domestically and internationally.

Description: The conduct of HIV research in the United States and abroad requires establishment of infrastructure to carry out this research program, including facilities and instrumentation, computers, data communications, laboratories, and animal colonies.

Action Steps: Support facilities to study animal models of pediatric AIDS.
Foster animal models to study HIV-related malignancies.

Support the Research Facilities Infrastructure Program (RFI) and General Clinical Research Centers (GCRC) Program.

Support use of the National Research and Education Network (NREN) for national and international collaboration and data communications.

Provide for expansion of breeding facilities to ensure the adequate supply of species of emerging importance, e.g. *M. nemestrina.*

Provide NCRR animal model support tied to needs of basic research grants.

Provide for the long-term support of advanced in-country research and research infrastructure in those developing countries participating in efficacy trials of candidate HIV vaccines and other priority intervention research.

Develop and support animal models predictive of human behavior, specifically, models of non-human primate behavior of impaired impulse control and risk-taking.

Support laboratory and biocontainment facilities for primate research.

Support the Internet connections program at health sciences centers and hospitals for research and patient care.

Establish and support repositories of samples obtained from individuals with HIV infection for current and future studies.

Increase support for screening the development of HIV macaque monkey models.

Develop and support Regional Primate Research Center (RPRC) expertise in molecular immunology, peptide biochemistry, and pharmacology.

Provide for the establishment of specific pathogen-free (SPF) non-human primate programs at all the RPRCs.

Provide further support for the development of SPF macaque colonies.

Resources:

FY 95: ~~$46,483,000 e~~ 46.5 million
FY 96: ~~$44,643,000 e~~ 44.6 million
FY 97: ~~$44,335,000 e~~ 44.3 million

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Agency: **Department of Justice**

Goal: To estimate the prevalence of HIV/AIDS among the corrections and parole population and to monitor the HIV/AIDS-related policies of Federal, State, and local correctional agencies.

Objective:

Data collection and dissemination of periodic reports.

Action Steps: Conduct surveys of federal, state and local prisons and inmates and publish results in periodic reports.

Descriptions: When published, the 1995 Survey on Probation, the 1996 Survey of Inmates in Local Jails, and the 1997 Survey of State and Local Federal Inmates in Adult Correctional Facilities will contain estimates of HIV prevalence among probationers and inmates, and characteristics of this HIV positive population.

Publication of reports describing findings of multi-year project, "HIV Education in Lockups and Booking Facilities."

1994 Survey of HIV/AIDS in Correctional Facilities.

Publication of 1996 report "HIV/AIDS and STDs in Juvenile Facilities."

Census of prison, survey of jail and prison inmates and probationers, and study examining research on prevention programs directed towards at persons whose behavior makes them vulnerable to HIV infection.

Resources:

FY 95: Part of overall operating budget.

FY 96: Part of overall operating budget.

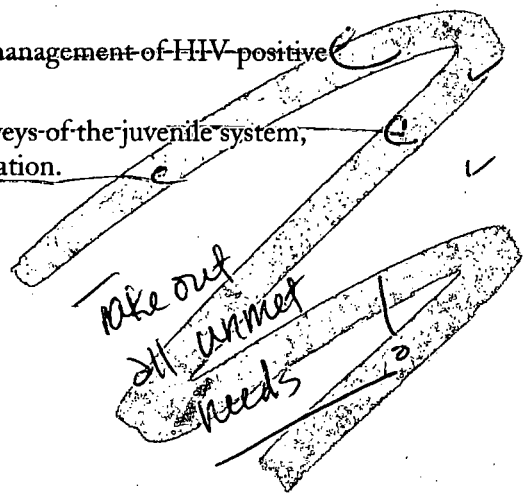
FY 97: Part of overall operating budget.

Populations Served: Department of Justice, corrections administrators, and public.

Constituency Involvement: None.

~~***Unmet Need:*** Funding for research into requirements for effective management of HIV-positive inmates.~~

~~Funding to conduct surveys of individual facilities and increase surveys of the juvenile system, and to conduct additional work in the areas of prevention and education.~~



~~Department of Justice, continued~~

Agency: Department of Veterans Affairs

Goal: To utilize the unique resource of the VA-served patient population to further biomedical, health services, and rehabilitation research on HIV and AIDS.

Objective 1:

Support AIDS-related research as a high priority area within the VA-served patient population utilizing the unique resources.

Action Steps: Fund research with high technical and scientific merit.

Continue to fund AIDS-related research through existing funding mechanisms, i.e., investigator-initiated studies, cooperative studies, and research centers.

Collaborate with other federal departments and agencies in initiating and conducting AIDS relevant research (including joint funding of projects), thereby making the unique resources of VA available to collaborating investigators.

Provide applicants for research support with feedback on the technical and scientific quality of their proposals.

Objective 2:

Develop and maintain AIDS Research Centers to stimulate and emphasize importance of HIV/AIDS research in VA's unique population.

Action Steps: Establish AIDS Research Centers based on competitive proposal basis.

Objective 3:

Encourage collaboration with other Federal departments and agencies in initiating and conducting AIDS-related research.

Action Steps: Facilitate investigator requested funding by NIH, other Federal agencies. Support participation in community trials on individual investigator and medical center basis.

Objective 4:

Disseminate research findings.

Action Steps: Publish and present findings of research in peer reviewed journals, and at national and international conferences.

Description: Research activities.

Resources:

FY 95: $ ~~5,400,000~~ * 5.4 million
FY 96: $ ~~5,700,000~~ * 5.7 million
FY 97: $ ~~5,700,000~~ * 5.7 million

(* Estimated expenditures for HIV/AIDS research are part of the general Medical and

Department of Veterans Affairs, continued

Prosthetics Research budgets. FY 1996 and FY 1007 estimates are based on the resource levels contained in the President's budget.)

Populations Served: Veteran patients, general public, researchers.

Constituency Involvement: Veteran patients, scientific community, general public at large.

Agency: Department of Treasury

Goal: Through tax code policies, provide incentives for privately-sponsored research, including HIV-related research.

Objective:

Encourage private sector investment in medical research, including HIV-related research.

Action Steps: Support the revenue neutral extension of the Research and Experimentation Tax Credit and the Orphan Drug Tax Credit.

Descriptions: Research and Experimentation (R&E) Tax Credit and Orphan Drug Tax Credit.

Resources:

FY 95: Not applicable.

FY 96: Not applicable.

FY 97: Not applicable.

Populations Served: Private sector entities supporting research.

Constituency Involvement: The National AIDS Drug Development Task Force, comprised of industry and government representatives and patient advocates, supported these policies.

Agency: Department of Commerce

Goal: To foster, serve, and promote the Nation's economic development and technological advancement, including encouraging HIV-related advances and innovation through the Department's collaborative efforts with the global business community.

Objective: Support activities which can assist in forwarding AIDS research by expanding the role of public-private partnerships in developing a vaccine and therapeutics.

Action Steps: Through the Advanced Technology Program (ATP), promote advances in biotechnology and provide funding to small and start-up research and development companies;

Support the Patent and Trademark Office's (PTO) AIDS-related patent database, developed in partnership with the National Science Foundation;

Through the National Technical Information Service, disseminate HIV-related training and technical materials;

Through data collection and analysis programs conducted by the Bureau of the Census and the Bureau of Economic Analysis, provide data for decision-making regarding the distribution of funds and other resources for private and public health initiatives, including HIV-related research, treatment, and service programs;

Through scientific standards, methodologies and technologies developed through the programs of the National Institute of Standards and Technology, set standards for laboratory procedures and equipment calibration at research facilities, including those conducting HIV-related research; and

Through the Patent and Trademark Office Biotechnology Examining Groups, review applications for a range of proposed HIV-related patents.

Descriptions: Advanced Technology Program, Patent and Trademark Office reviews, National Technical Information Service, Bureau of the Census, and the National Institute of Standards and Technology.

FY 95: Part of overall operating budget
FY 96: Part of overall operating budget
FY 97: Part of overall operating budget

Populations Served: Start-up companies, biotechnology and pharmaceutical companies, academic institutions, and researchers.

Constituency Involvement: The Department supports public-private partnerships to encourage innovative research.

Unmet Need: An increase in support for valuable programs such as ATP and the Patent and Trademark Office's innovative AIDS-related patent database would enhance Department of Commerce's ability to serve both public and private sectors.

Agency: Department of Defense

Goal: To carry out state-of-the-art research on the prevention and treatment of HIV infection to promote medical readiness in U.S. military forces.

Objectives: Support the development of a safe and effective HIV vaccine.

Support the development of new biochemical and genetic strategies to slow HIV disease progression

Support natural history studies for the purpose of evaluating the efficacy of intervention strategies.

Action Steps: Define the global molecular epidemiology of HIV to assist with candidate vaccine selection.

Explore novel vaccine technologies.

Conduct vaccine trials in endemic areas.

Assess the immune response and efficacy of vaccine candidates.

Evaluate potential therapies for treatment of HIV infection and potential for immune reconstitution.

Evaluate prevalence of drug resistance, develop rapid genetic assay for resistant mutants, and methods for genetic targeting of novel therapies *in vivo*.

Participate in national surveillance of AZT resistance.

Develop a comprehensive panel of immunologic, virologic, and functional parameters for management of HIV infection.

Support natural history studies and specimen repositories.

Descriptions: Vaccine, therapeutic, and epidemiological research, including vaccine design, development and testing in the U.S. and overseas locations; epidemiologic studies of vaccine field studies; and reduction or conclusion of drug treatment and behavior studies.

FY 95: $37,000,000
FY 96: $26,600,000
FY 97: $ 9,611,000

Populations Served: Active duty personnel.

Constituency Involvement: Clinicians, researchers, and active duty personnel.

Unmet Need: Increased resources would permit more aggressive research on promising therapies and vaccine candidates.

Agency: Department of Energy

Goal: To provide infrastructure support for physical chemical research, termed structural biology, including indirect support for HIV-related research.

Objective: In collaboration with other Federal agencies, provide access to sophisticated equipment and specially trained scientific personnel.

Action Steps: In collaboration with all relevant agencies (NIH, NSF) and the scientists they support, provide continued essential support for structural chemistry and biology facilities. Provide both the academic and the industrial community access to the facilities for further studies on the structural biology of HIV.

Descriptions: The National Synchrotron Light Source at Brookhaven National Laboratory includes a Department of Energy (DOE) supported x-ray beam line extensively used by structural biologists studying virus structure, including the structure of HIV. In addition, through its National Laboratory system, DOE provides user facilities at other synchrotron light sources and at neutron beam facilities, which can be used by researchers to characterize the structural configuration of intact HIV , and HIV's biochemical components, often in complexes with inhibitors. These studies assist in the development of novel therapies, as well as advance our understanding of the pathogenesis and fundamental biology of HIV growth.

FY 95: Part of DOE's general operating budget.
FY 96: Part of DOE's general operating budget.
FY 97: Part of DOE's general operating budget.

Populations Served: The scientific community.

Constituency Involvement: Access to resources through peer review.

Unmet Need: Stable funding, guaranteed access for scientists to the facilities for the foreseeable future.

Agency: Department of Health and Human Services, Agency for Health Care Policy and Research

Goal: To provide national estimates of the cost and use of HIV-related medical and non-medical services.

Objective 1: To provide comprehensive information on unmet needs for service and barriers to accessing services.

To examine effects of different systems of organizing and delivering care on outcomes such as cost, utilization, survival, patient satisfaction, and quality of life.

To examine effects of patient characteristics (including gender, race/ethnicity, substance abuse, mental health, socioeconomic status, insurance coverage) on outcomes such as service utilization, unmet service needs, and costs.

To provide data on service utilization and costs for a representative sample of rural residents with HIV infection.

To examine patterns of transition between different types of provider (e.g., private physician to public clinic) and the relationship of such transitions to changes in clinical status, employment, and insurance coverage.

Action Steps: This study will be the first to obtain a true national random sample of people with HIV infection receiving treatment. Approximately 3200 adult patients in urban and rural areas will be enrolled. Study will be co-sponsored by HRSA, NIMH, NIDR, NIA, NIDA, and the Robert Wood Johnson Foundation.

Descriptions: HIV Costs and Service Utilization Study (HCSUS)

FY 95: $4,150,657
FY 96: $3,468,114
FY 97: $3,131,582

Populations Served: HIV-infected individuals receiving treatment.

Constituency Involvement: Community Advisory Board, comprising members of infected and affected groups, has been established.

Unmet Need: Insufficient resources for a national probability sample of pediatric HIV-infected patients. Insufficient resources for a sample of HIV-infected adolescents.

Objective 2: To examine health care utilization among

participants in the NIH-sponsored Women's Interagency HIV Study (WIHS).

Action Steps: Supplement the WIHS by adding a health services research component.

Collect and analyze utilization data on women with HIV infection (in addition to the detailed clinical data obtained in the core study.)

Descriptions: Women's Interagency HIV Study (WIHS)

FY 95: $60,000
FY 96: $0
FY 97: $0

Populations Served: Women with HIV infection participating in the WIHS.

Constituency Involvement: A broad representation of researchers and patient advocates had input in the development of the WIHS.

Unmet Need: None.

Objective 3: To examine factors affecting health care utilization among participants in the NIH-sponsored Multicenter AIDS Cohort Study (MACS).

Action Steps: Supplement the MACS by adding a health services research component.

Collect and analyze utilization data on men with HIV infection (in addition to the detailed clinical data obtained in the core study).

Descriptions: Multicenter AIDS Cohort Study (MACS)

FY 95: $65,000
FY 96: $0
FY 97: $0

Populations Served: Homosexual and bisexual men participating in the MACS in four urban areas.

Constituency Involvement: A broad representation of researchers and patient advocates had input in the development of the MACS.

Unmet Need: None

Objective 4: To examine health care utilization among participants in the CDC-sponsored HIV Epidemiological Research Study (HERS).

Action Steps: Supplement the HERS by adding a health services research component.

Collect and analyze utilization data on women with HIV infection (in addition to the detailed clinical data obtained in the core study).

Descriptions: HIV Epidemiological Research Study (HERS)

FY 95: $50,000
FY 96: $50,000
FY 97: $50,000

Populations Served: Women with HIV infection participating in the HERS.

Constituency Involvement: A broad representation of researchers and patient advocates had input in the development of the HERS.

Unmet Need: None.

Objective 5: To provide longitudinal data on utilization of inpatient, outpatient, home care, pharmaceutical, and other services, and to estimate their associated costs.

To examine the impact of a Medicaid Home and Community-Based waiver on service utilization, costs, functional status, and survival.

To examine any substitutions of formal for informal home care.

Action Steps: Conduct interviews with participants in New Jersey Medicaid Waiver program.

Abstract data from Medicaid claims.

Descriptions: Health Care Costs and Utilization in AIDS Home Care.

FY 95: $295,918
FY 96: $39,456
FY 97: $0

Populations Served: Medicaid recipients with AIDS in New Jersey.

Constituency Involvement: Persons with AIDS residing at home or in community facilities.

Unmet Need: None.

Objective 6: To examine types of ambulatory care providers used to treat HIV infection, patterns of transitions between ambulatory provider types, and service utilization and costs for pediatric HIV patients.

Action Steps: Analyze Medicaid claims and eligibility data from New York State Medicaid files.

Descriptions: Ambulatory Care for HIV/AIDS, Models and Outcomes.

FY 95: Part of overall operating budget.
FY 96: Part of overall operating budget.
FY 97: Part of overall operating budget.

Populations Served: New York State Medicaid recipients.

Constituency Involvement: NA

Unmet Need: None.

Objective 7: To assess the impact of antiretroviral, antimicrobial, and prophylactic treatment on the natural history of HIV infection, and the effect of pharmaceutical therapies on service utilization, costs, and clinical outcomes.

Action Steps: Develop clinical database linked to Medicaid claims data.

Descriptions: Outcomes of Pharmaceutical Therapy in HIV Disease.

FY 95: $527,497
FY 96: $479,952
FY 97: $505,000

Populations Served: HIV-infected population in Maryland.

Constituency Involvement: NA

Unmet Need: None.

Objective 8: To study issues of costs and quality of care, with a focus on women and children, examine trends and variation in adherence to scientifically-based clinical guidelines, and study

predictors of variation in treatment, by patient, physician, and practice setting characteristics.

Action Steps: Analyze Medicaid claims and eligibility data, supplemented with AIDS Registry data.

Descriptions: Quality and Costs of Care for HIV Infected Medicaid Patients.

FY 95: Part of overall operating budget.
FY 96: Part of overall operating budget.
FY 97: Part of overall operating budget.

Populations Served: New Jersey Medicaid recipients.

Constituency Involvement: NA

Unmet Need: None.

Objective 9: To develop an econometric framework for the simultaneous study of health care usage and survival, and synthetic estimates of per-person lifetime costs of HIV disease for various groups of HIV-infected individuals.

Action Steps: Formulate statistical models and associated computer software.

Descriptions: Developing Econometric Models to Estimate AIDS Costs.

FY 95: $248,126
FY 96: $8,003
FY 97: $0

Populations Served: Participants in the AIDS Costs and Service Utilization Survey, with potential extensions to all persons with HIV disease.

Constituency Involvement: NA

Unmet Need: None.

Objective 10: To identify personal and institutional factors that shape physicians' willingness to care for HIV-infected patients.

Action Steps: Conduct the third in a series of interviews with physicians, who are currently in their sixth post-graduate year.

Descriptions: Determinants of Physicians' AIDS-Related Practice Behavior

FY 95: Part of overall operating budget.
FY 96: Part of overall operating budget.
FY 97: Part of overall operating budget.

Populations Served: Persons with AIDS

Constituency Involvement: Physicians

Unmet Need: None.

Objective 11: Continuing work previously completed with AHCPR support, compare outcomes of inpatient care for AIDS provided by dedicated AIDS units versus scattered-bed approaches.

Action Steps: Expand upon original comparative multi-site observational study of 20 hospitals.

Descriptions: Outcomes of Hospital Dedicated AIDS Units

FY 95: $180,649
FY 96: $214,708
FY 97: $0

Populations Served: 1300 patients receiving services in study hospitals.

Constituency Involvement: NA

Unmet Need: None.

Objective 12: Obtain and analyze data on inpatient hospital utilization by people with HIV infection.

Action Steps: Assemble and will analyze database of hospital discharge data from all hospitals in 12 States.

Descriptions: Hospital Cost and Utilization Project

FY 95: $500,000
FY 96: $0
FY 97: $500,000

Populations Served: Patients with AIDS receiving inpatient care in hospitals in 12 states.

Constituency Involvement: NA

Unmet Need: None.

Objective 13: To examine access to primary medical care for HIV positive African Americans who are linked to health services through community-based case management.

To improve access to primary medical care for HIV positive African Americans.

To create a model of assessment of primary health care access that could be utilized in other urban African-American communities.

Action Steps: In-depth structured interviews, unstructured interviews, focus groups, participant observation and direct observation.

Description: Study entitled "Access to Primary Health Care for HIV+ African Americans".

FY 95: $21,600
FY 96: $0
FY 97: $0

Populations Served: African-American and Euro-American clients in the greater Tampa metropolitan area.

Constituency Involvement: New clients at three ethnically diverse community-based case management sites.

Unmet Need: None.

Objective 14: To develop better conceptual and operational delineation of "health care related trust".

To describe the factors that potentiate or mitigate trust among HIV positive and HIV negative inmates.

To determine the effect of trust on health seeking behavior and adherence to medical therapy among HIV positive inmates.

Action Steps: In-Depth interviews, focus group discussions, and administration of standardized surveys to inmates.

Description: Study entitled "Trust and HIV-Related Health Behavior Among Connecticut Inmates".

FY 95: $21,600
FY 96: $0
FY 97: $0

Populations Served: Prisoners in Connecticut.

Constituency Involvement: HIV positive inmates in treatment, HIV positive inmates not in treatment, and HIV negative inmates.

Unmet Need: None.

Objective 15: To gain an understanding of the health values and the determinants of health values of HIV positive patients.

Action Steps: Conduct focus groups, pose standard gamble, time tradeoff, and rating scale questions, and conduct intensive individual interviews.

Description: Study entitled "Understanding Health Values of HIV-infected Patients".

FY 95: $0
FY 96: $160,160
FY 97: $0

Population Served: HIV-positive patients

Constituency Involvement: Patients will be recruited from a university-based AIDS treatment center which serves nearly all HIV positive patients in the study area.

Unmet Need: None.

Agency: Department and Health and Human Services, Food and Drug Administration

Goal: To ensure the safety and effectiveness of HIV-related therapeutic agents.

Objective: Expedite access and approval of safe and effective drugs and biologics.

Action Steps: Encourage quality applications and data submissions to review division to ensure timely and efficient pre- and postmarket review.

Descriptions: Conduct meetings with sponsors to discuss drug development plans, expanded access programs, and accelerated approval options.

Facilitate scientific review of drugs and biologics by FDA advisory committees.

FY 95: $25,235,000
FY 96: $25,235,000
FY 97: $25,235,000

Populations Served: All persons who may benefit from approved therapeutic agents.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry and patient advocates.

Unmet Need: With the passage of Prescription Drug Use Fee Act of 1992, the FDA has been able to expeditiously review HIV/AIDS related therapeutic applications. With the continuation of the provisions in the Act, the FDA will be able to continue expeditious reviews.

Agency: Department of Health and Human Services, Food and Drug Administration

Goal: To ensure the safety and effectiveness of HIV-related preventive and therapeutic vaccines.

Objective: Expedite regulatory review of promising products for preventive and therapeutic vaccines.

Action Steps: Expand partnership between FDA and its counterparts from outside organizations involved in vaccine development.

Descriptions: Encourage early consultation with sponsoring companies, develop guidance documents, exchange information, and work with other agencies and international organizations. Facilitate scientific review by FDA advisory committees.

FY 95: $11,863,000
FY 96: $11,863,000
FY 97: $11,863,000

Populations Served: All persons who may benefit from approved preventive and therapeutic vaccines.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Unmet Need: With the passage of Prescription Drug Use Fee Act of 1992, the FDA has been able to expeditiously review HIV/AIDS related therapeutic applications. With the continuation of the provisions in the Act, the FDA will be able to continue expeditious reviews.

Agency: Department of Health and Human Services, Food and Drug Administration

Goal: To ensure the effectiveness of test methodologies for HIV detection and measurement.

Objective: Expedite improved test methodologies (such as diagnostic reagents and test kits) for HIV detection, confirmation, and viral load measurement.

Action Steps: Ensure timely and efficient pre- and postmarket review.

Descriptions: Encourage early consultation with sponsor and develop guidance documents. Facilitate scientific review of drugs and biologics by FDA advisory committees.

FY 95: $8,732,000
FY 96: $8,732,000
FY 97: $8,732,000

Populations Served: All persons who may benefit from approved test methodologies for HIV detection and measurement.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Unmet Need: With the passage of Prescription Drug Use Fee Act of 1992, the FDA has been able to expeditiously review HIV/AIDS related therapeutic applications. With the continuation of the provisions in the Act, the FDA will be able to continue expeditious reviews.

Agency: Department of Health and Human Services, Food and Drug Administration

Goal: To ensure the safety and effectiveness of HIV-related medical devices.

Objective: Expedited access and approval of safe and effective medical devices.

Action Steps: Encourage quality application and data submissions to ensure timely and efficient pre- and postmarket review.

Descriptions: Conduct meetings with sponsors on study design; produce guidance documents. Facilitate scientific review of drugs and biologics by FDA advisory committees.

FY 95: $9,457,000
FY 96: $9,457,000
FY 97: $9,457,000

Populations Served: All persons who may benefit from approved HIV-related medical devices.

Constituency Involvement: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Unmet Need: The FDA depends on scientific advisory committees to provide independent expert advice to the agency in its evaluation of regulated products. These committees are composed of representatives from academia, research, government, industry, and patient advocates.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To conduct and support natural history and epidemiological research to improve the understanding of the risk factors and mechanisms of HIV transmission and disease progression and to develop prevention strategies to reduce or prevent HIV transmission.

Objective 1: Develop and assess intervention strategies to reduce or prevent HIV transmission in both domestic and international settings.

Action Steps: Develop and maintain the infrastructures to define populations in the United States and throughout the world with incidence and prevalence suitable for vaccine and other intervention trials (e.g. microbicides, barriers, treatment, behavioral) for preventing HIV transmission.

Support development and evaluation of improved, acceptable, effective physical and chemical barrier methods and conduct research on existing barrier methods to prevent sexual transmission of HIV and STDs.

Develop strategies and conduct studies to evaluate vaccines, drugs, and other interventions such as caesarian sections, vaginal cleansing, breast-feeding practices, nutritional interventions, and other approaches that prevent perinatal transmission.

Develop and assess the efficacy of strategies that may decrease transmission of HIV among drug users.

Develop and evaluate biological and behavioral interventions to control STDs as co-factors in HIV transmission.

Develop strategies that enhance safe sex behaviors and provide information on safe and effective contraceptive choices for at-risk women.

Develop methods to prevent infection in hard-to-reach gay male populations such as young, substance-using, and minority gay and bisexual men.

Develop methods of accessing hard-to-reach populations to identify factors that contribute to recruitment (and retention) into prevention and intervention activities.

Evaluate access to, acceptability of, and compliance with interventions such as AZT for perinatal transmission, condoms, and virucides.

Evaluate improved procedures for screening, monitoring, and inactivating HIV and other retroviruses in the blood supply; and develop and evaluate alternatives to blood transfusion.

Assess the impact of drug and alcohol abuse and mental health impairment on efficacy of behavior modification interventions directed at sexual transmission.

Develop effective drug treatment strategies for addiction, particularly focused on heroin and cocaine use.

Description: The development of biologically based interventions to interrupt transmission is an essential component of a comprehensive HIV prevention strategy that also includes behavioral intervention strategies as well as efforts to develop a vaccine(s). International studies should be supported with the goal of developing prevention strategies that can be used to reduce HIV transmission in the United States. Research is ongoing in these areas.

Epidemiologic studies, including vaccine preparedness research, provide opportunities for intervention research in defined cohorts of well-characterized populations. Strategies that employ therapies, devices, and other approaches, such as needle/syringe exchange programs using HIV seroconversion end points, are useful approaches for providing epidemiologic causation and evaluating effectiveness in preventing or reducing HIV transmission.

In addition, despite the fact that the blood supply in the United States is safer than it has ever been, it is important to develop even better methods for maintaining and improving its safety.

Objective 2: Characterize the risk factors and mechanisms of HIV transmission in both domestic and international populations, with the goal of preventing transmission.

Action Steps: Evaluate HIV transmission in relationship to: viral factors such as virus load in the blood and at mucosal sites, characteristics of HIV (genotype and phenotype), and pre-existing infection with other agents; host factors such as contraceptives, pregnancy, menstrual cycle, substance abuse, and nutritional, immunologic and genetic determinants; local factors including intercurrent STDs, exogenous irritants, oral and anogenital

inflammation, mucosal immunity, circumcision and cervical ecotopy.

Further define the timing and mechanisms and risk factors in perinatal transmission, including breast-feeding.

Study mechanisms of resistance to HIV infection in persons who remain uninfected despite perinatal, sexual or parenteral exposure.

Define the determinants of high-risk behavior for transmission through drug use and sexual practices.

Characterize the dynamics of HIV transmission in epidemiologic studies of at-risk groups, including evaluation of sexual and drug-using networks, social and geographic mixing patterns, and turnover rates of at-risk populations.

Characterize the transmission and host immune responses of related retroviruses.

Description: Understanding the role of risk factors and mechanisms of HIV transmission is critical to the development of biologically and behaviorally based strategies to interrupt transmission of HIV. Epidemiologic studies provide important biological and behavioral information including the role of co-factors that may reduce or enhance transmissibility.

Objective 3: Elucidate the progression of HIV infection, from its earliest stages through long-term sequelae, with the goal of understanding, preventing, and treating those factors.

Action Steps: Use epidemiologic studies to identify pathogenic mechanisms and co-factors for disease progression and disease-specific outcomes in well-defined subsets of individuals, individuals, including those with different rates of progression.

Conduct epidemiologic studies to understand the initiation and progression of early HIV infection, according to route of exposure, viral dose, viral genotype and phenotype, and host response, and how these early events influence disease progression.

Use epidemiologic studies to investigate the influence of viral genotype and phenotype on transmission efficacy and disease progression.

Use epidemiologic studies to evaluate the extent of dissemination

of drug-resistant strains of HIV and its impact on pathogenesis.

Study the natural history of related retroviruses to elucidate retroviral pathogenesis.

Elucidate the mechanisms of HIV-associated carcinogenesis to improve strategies for early diagnosis and intervention.

Study HIV-infected children to determine: (1)mechanisms that contribute to impaired growth and neurodevelopment;(2)impact on childhood infectious diseases and the safety and efficacy of immunization;(3)impact on childhood psychosocial development, and (4)childhood-specific complications.

Evaluate the interaction of hormonal factors (including pregnancy, contraceptives, and hormonal replacement therapy) and HIV disease progression.

Study the progression of HIV-related disease in adolescents who have acquired their diseases as a result of drug use and/or sexual activity.

Study the natural history of HIV infection in the nervous system, including cognitive impairment, dementia, and neuropathy.

Describe the full spectrum of HIV-related diseases in HIV-infected populations.

Maintain and effectively utilize national specimen repositories for HIV-related studies.

Description: Epidemiologic studies provide a critical knowledge and resource base for more basic investigations of HIV pathogenesis. A better understanding of the diversity of HIV-related disease outcomes, co-factors for progression, and predictors of disease progression will be important in furthering attempts to develop HIV vaccines and more effective therapeutic interventions against HIV and its sequelae.

Objective 4: Undertake epidemiologic research to reduce or prevent the occurrence of opportunistic illness in HIV-infected persons.

Action Steps: Study the impact of HIV infection on the emergence of new human pathogens and the impact of HIV infection on the reemergence of infectious diseases domestically and internationally.

Identify risk factors for the acquisition of opportunistic pathogens.

Study the determinants of the continuing occurrence of preventable opportunistic illnesses.

Study the role of transmissible and other preventable exposures in the etiology of AIDS-associated cancers and other outcomes.

Description: Most morbidity and mortality in HIV-infected persons result from the occurrence of opportunistic illnesses, including both infections and malignancies. Strategies to prevent these illnesses include prevention of exposure to the etiologic agents, prevention of disease in those who are exposed, and prevention of disease recurrence. Additional epidemiologic data are needed to design more effective strategies to prevent the occurrence of these opportunistic illnesses.

Objective 5: Develop and evaluate new laboratory assays, behavioral methods, and statistical techniques for epidemiologic studies.

Action Steps: Promote development and evaluation of virologic and immunologic assays to elucidate mechanisms of HIV transmission and disease.

Develop new survey and interview techniques to better measure HIV risk behaviors.

Develop new biostatistical techniques, including mathematical models, to better characterize transmission dynamics and disease progression.

Develop innovative approaches for record linkages to study HIV-associated diseases and mortality.

Characterize the epidemiologic features of emerging HIV variants, including drug-resistant strains, diverse genotypes, and newly recognized geographic distribution.

Description: Epidemiologically defined populations contain well-characterized cohorts that can provide insights into HIV transmission, including resistance and susceptibility to infection and infectiousness, and into progression of HIV-related disease, from early infection through long-term sequelae, including cancer and neurocognitive impairment. The application of innovative biomedical research and behavioral strategies to such populations will greatly increase understanding at the

biological level and will help to identify strategies for prevention of transmission and for clinical management of patients.

FY 95: $192,624,000
FY 96: $205,812,000
FY 97: $203,285,000

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Unmet Needs: The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $33,986,000 over the FY 1997 figure.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To conduct and support research to improve the understanding of HIV and the pathogenic mechanisms of HIV disease.

Objective 1: Delineate the cellular and molecular mechanisms associated with the viral immunopathogenesis of HIV-related immune dysfunction.

Action Steps: Delineate the direct and indirect mechanisms underlying HIV-induced depletion and dysfunction of target cells/tissues.

Define the virologic (load, phenotype, and genotype), immunologic (specific and nonspecific), pharmacologic, and environmental factors that contribute to disease progression and non-progression.

Delineate the mechanisms of virally triggered immunopathogenesis, including immune activation, induction of nonresponsiveness, and production of host factors, including cytokines, in pathogenesis.

Delineate the molecular mechanisms by which virus-encoded genes, gene products, and cellular factors regulate HIV replication and influence pathogenesis, with special emphasis on the use of primary virus isolates and cells.

Delineate the mechanisms of host genetic factors that mediate resistance or sensitivity to infection and influence disease progression.

Delineate the physiology and HIV-related pathophysiology of primary and secondary lymphoid organs, including hematopoietic precursor cells and their microenvironment.

Study the mechanisms of HIV infection that uniquely influence the developing immune system.

Further develop and utilize experimental models to examine the pathogenesis of lentiviral infections.

Establish and expand programs to facilitate access to and sharing of key patient samples, animal model resources, laboratory reagents, information databases, and quantitative virologic and immunologic assays.

Description: Basic scientific information regarding the cellular and molecular mechanisms that underlie HIV-related immune dysfunction and viral pathogenesis is critical to all areas of AIDS research.

Objective 2: Delineate the molecular and cellular mechanisms of transmission and establishment of infection and their impact on disease progression.

Action Steps: Define the cellular and immune mechanisms that inhibit/enhance the early events in establishing HIV infection.

Determine the impact of early events in the establishment of HIV infection on the clinical course of the disease.

Determine the roles of specific and nonspecific mucosal and systemic immunity and other host factors that inhibit/enhance HIV transmission.

Determine the cell or tissue type that serves as the portal of entry of HIV and the impact of STDs and other pathogenic processes that influence HIV transmission.

Determine the role of viral phenotype/genotype and load on transmission of cell-free and cell-associated virus.

Elucidate unique aspects of HIV transmission and disease progression in under-researched populations.

Determine the mechanisms of vertical HIV transmission.

Description: The mechanisms of HIV transmission and the early events in the establishment of infection, and their relationship to disease progression, need to be better understood.

Objective 3: Elucidate the etiologic factors and co-factors in the pathogenesis of AIDS-associated disease states. Enhance a bidirectional flow between basic and clinical observations and intervention programs ion HIV-related complications and foster interdisciplinary collaborations.

Description: Knowledge of AIDS-associated disease pathogenesis is urgently needed.

Sub-Objective 3a: Elucidate the etiologic factors, co-factors, and mechanisms in the pathogenesis of HIV-related malignancies.

Description: Knowledge about the origins and pathogenesis of HIV-

related cancers is urgently needed.

Action Steps: Elucidate the role of HIV infection, immune dysfunction, and interactions with potential co-factors in the development of HIV-associated malignancies.

Identify the characteristics of the host that predispose to development of malignant disease, including genetic, hormonal, and growth factors and immunologic characteristics.

Identify the pathogenic contributions of oncogenes, suppressor genes, carcinogens, and non-HIV viral and other microbial genes and proteins to HIV-associated malignancies; correlate these molecular factors with epidemiologic studies.

Establish and expand programs to facilitate development and sharing of *in vivo* animal models and patient specimens for HIV-associated malignancies.

Sub-objective 3b: Elucidate the pathogenic mechanisms involved in HIV-associated neurological disease and neurobehavioral dysfunction.

Description: The damage that leads to both central and peripheral nervous system dysfunction must be better understood through studies of HIV-associated neuropathogenesis.

Action Steps: Investigate the characteristics of lentiviruses that invade the nervous system and the mechanisms by which these viruses cause nervous system impairment.

Study the effects of neurotrophins and immunoregulatory and proinflammatory cytokines on both host and viral gene expression.

Employ animal models of CNS-lentivirus infection that are crucial to understanding neuropathophysiology.

Delineate the role of OIs and drug treatment in neurologic complications of AIDS, including CNS dysfunction and peripheral neuropathies.

Investigate biological and environmental factors that may affect nervous system function in the context of HIV-1 infection, emphasizing the role of psychoactive drug use.

Study mechanisms of HIV infection that uniquely influence the developing nervous system.

Develop technologies for correlative structural-functional analysis of progressive HIV-associated neurological and behavioral disorders and the progression of CNS disease.

Sub-objective: Elucidate the pathogenic mechanisms of HIV-related opportunistic infections.

Description: It is critical to understand the pathogenic mechanisms responsible for the development of HIV-associated OIs.

Actions Steps: Elucidate the mechanisms of immune function that mediate protection against OIs.

Study the effects of OIs on immune dysfunction and HIV disease progression.

Conduct studies of the basic biology and pathogenic mechanisms of opportunistic pathogens and their interactions with the host.

Develop *in vitro* techniques and animal models to propagate the opportunistic pathogens associated with HIV disease.

Develop and validate diagnostic assays for the reliable and rapid identification of HIV-associated OIs.

Identify biologic markers that are correlative for susceptibility and disease progression for HIV-associated OIs.

Identify and elucidate the genetic and environmental risk factors associated with susceptibility to and development and progression of OIs.

Sub-objective 3c: Elucidate the etiology and pathogenesis of HIV-related disorders: gastrointestinal, renal, endocrine, cardiovascular, cutaneous, hematologic, oral, pulmonary, and other diseases.

Description: It is critical to understand various other organ/tissue-specific complications of HIV infection.

Action Steps: Investigate the etiologic and pathogenic mechanisms of HIV-associated gastrointestinal disease.

Identify the etiologic and pathogenic mechanisms of HIV-associated nephropathy.

Elucidate the etiology and pathogenesis of endocrine dysfunction and the role of alteration in the endocrine/immune axis in

progression of HIV disease.

Elucidate the etiology and pathogenesis of HIV-related autoimmune disorders and cardiovascular, cutaneous, hematologic, oral, pulmonary, and other organ/tissue-specific disorders.

FY 95: $344,303,000
FY 96: $382,903,000
FY 97: $400,182,000

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Unmet Needs: The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $20,801,000 over the FY 1997 figure.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To conduct and support preclinical and clinical research to develop, test, and optimize treatments for HIV infection, HIV-associated conditions, and for the prevention of HIV transmission.

Objective 1: Improve understanding of the structure and function of molecular targets in order to develop improved assays for such targets; conduct screening, discovery, and preclinical development of novel anti-HIV agents and strategies (such as gene transfer technology and interruption of transmission) directed to the virus and/or host cell; and foster activity by and in collaboration with industry.

Description: Identify and develop novel anti-HIV therapies, particularly those therapies that impact at different stages of the life cycle of the virus.

Action Steps: Identify and characterize promising targets for anti-HIV therapy and extend knowledge of their mechanisms of action, develop relevant assays for identifying drugs active against those targets, and develop new compounds active at those targets, with emphasis placed on identifying agents active at novel targets other than reverse transcriptase inhibitors; emphasize agents that can effectively cross the blood-brain barrier.

Complete preclinical development, in cooperation with industry when appropriate, of promising new compounds and combinations of compounds and novel natural products, including assessment of toxicity, immunologic effects, pharmacokinetics, teratogenicity, and fertility in animal models and development of analytical method and chemical formulations.

Continue and accelerate domestic and international collection screening of large numbers of natural and synthesized compounds for anti-HIV activity, with a particular emphasis on the detection of agents that act at unique steps of the HIV life cycle with the intent of identifying lead compounds that can be modified for increased potency and other attributes (such as bioavailability and central nervous system penetration); develop and screen combinatorial libraries.

Emphasize basic and applied research to advance cross-NIH development of gene therapy; support development of preclinical laboratories to advance gene therapies; advance gene therapies,

including new strategies for streamlining or eliminating ex vivo manipulation of cells; develop more efficient and safe viral and non-viral gene delivery vectors; target tissue cells and subcellular compartments; develop effective antiviral genes; standardize evaluation of different gene therapies singly and in combination; and develop suitable lentivirus animal models for in vivo efficacy and safety studies.

Determine the high-resolution molecular structures for several of the HIV proteins and apply these structures to the rational design of drugs as part of the targeted drug development program; determine generalizable and effective approached for the use of macromolecular structure in designing drugs to combat HIV infection and AIDS; make resolved structures available in publicly accessible data bases.

Increase understanding of the mechanisms and limitations of drug resistance; study the effect of various agents on HIV replication and viral variation; evaluate early markers of resistance; evaluate the activity of anti-HIV drugs in various cell types (including macrophages) and in various stages of the cell cycle.

Develop new compounds capable of inhibiting the sexual transmission of HIV, such as topical microbicides (which may inhibit HIV and STDs associated with enhanced HIV transmission), HIV-specific viricides, and systemic agents.

Develop formulations that would be suitable for infants and children for both existing and experimental agents.

Evaluate transplacental passage of antiretroviral and other agents as well as the effects of these drugs on placental function and on the embryo/fetus in animal models.

Objective 2: Conduct clinical trials and develop new trial methodologies for the treatment of HIV infection. Trials should be designed in order to rapidly develop new therapeutic strategies, optimize clinical efficacy and proper use of available modalities, define factors that affect the success of therapeutic strategies (including the role of resistance), and advance our understanding of disease pathogenesis and progression.

Description: Trials to evaluate new antiretroviral therapies alone and in combination will provide important information regarding resistance and synergistic effects of drugs that may eventually prolong the disease-free state and survival in HIV-infected individuals.

Action Steps: Support and improve clinical trials of potential therapeutic agents and combinations of agents in studies to determine pharmacokinetics and bioavailability and evaluate anti-HIV combinations that are non-cross-resistant, synergistic, and toxicity-sparing and that may delay development of drug-resistant HIV strains; enhance collaboration between and within ICDs to facilitate opportunities for clinical trials.

Implement the development and evaluation of virologic, immunologic, and clinical markers to assess drug activity and determine the prognostic value of surrogate markers in response to therapeutic interventions.

Support research and development of clinical trials methodology and study design so that appropriate pathways are taken rapidly to evaluate the activity, clinical efficacy, and ultimate acceptability of new agents and approaches that translate into clinical use.

Increase the understanding of the pathogenesis of HIV disease based on the evaluation of antiretroviral agents in clinical trials; establish effective mechanisms to evaluate therapeutic interventions and elucidate the pathogenesis of acute/early HIV infection.

Foster collaboration and better interactions with industry in drug development and evaluation efforts.

Evaluate safety, toxicity, and pharmacokinetics of retroviral agents provided to pregnant women, including transplacental passage of the agent, safety to the fetus/infant, and pharmacokinetics of drug elimination in the newborn. (Also noteworthy, assess the potential efficacy and feasibility of obstetric interventions to prevent vertical transmissions, such as cesarean deliveries and other aspects of intrapartum care.)

Enhance utilization of General Clinical Research Centers (GCRCs) for the conduct of single and multi-institutional clinical trials.

Develop and validate quality-of-life parameters included in patient assessments of clinical trials.

Support research on the effectiveness of pharmacologic (including compliance with therapies and STD prevention) and non-pharmacologic including psychosocial) interventions (including nutritional factors and adherence improvement).

Investigate possible interactions between therapies for HIV-related disease and other substances that HIV-infected individuals might use, such as drug-abuse treatment medications, oral contraceptives or other prescription drugs, nonprescription drugs, alternative or complementary therapies, or drugs of abuse.

Coordinate studies to encourage co-enrollment of patients on all trials where appropriate (co-enrollment would not only allow for better utilization of limited resources but also enable assessment of concomitant medications and their interactions, improving the efficiency of the primary study).

Develop a coordinated plan to evaluate long-term therapeutic strategies, e.g., develop plans for long-term follow-up, enroll patients in sequential randomized trials once they have reached an end point in their initial trial.

Support clinical trials to evaluate the safety and pharmacokinetics of existing and experimental agents for use in treating HIV-infected infants and children; evaluate the effects of puberty on the pharmacokinetics of antiretroviral agents and other drugs for the treatment/prophylaxis of HIV infection and the pharmacokinetics of drugs in adolescents.

Evaluate potential late toxic effects of antiretroviral therapy given to infants and children.

Objective 3: Develop and evaluate strategies that will enhance, restore, and/or maintain the immune systems of HIV-infected individuals and extend our understanding of immunopathogenesis.

Description: Essential to HIV research efforts are studies directed toward finding therapies that can restore, enhance, or maintain the integrity of the immune system.

Action Steps: Evaluate therapeutic approaches that test specific hypotheses of HIV immunopathogenesis,

Develop and validate new methods for evaluating immune function in the context of clinical trials.

Continue and accelerate the testing of cytokines, modulators of cytokines, and other immunomodulating agents either singly or in combination with antiretroviral agents for the purpose of reconstituting the deficient immune systems of HIV-infected individuals.

Develop and evaluate various approaches of active and passive

immunotherapy for both HIV infection and its sequelae.

Develop a program of reconstituting the immune systems of HIV-infected individuals by administration of cellular elements in an autologous, syngeneic, or allogeneic fashion, including use of expanded peripheral blood T cells, bone marrow transplantation, thymic transplantation, cord blood, stem cells, and/or xenogeneic transplantation.

Develop new therapeutic strategies based on gene therapy approaches to protect hematopoietic stem cells and thereby reconstitute the immune system with HIV-resistant lymphoid, monocytic and other cellular compartments.

Use structural biologic techniques to determine the structures of various cytokines and cytokine receptors as potential targets for HIV therapies.

Increase collaboration of ICDs by joint funding of projects to facilitate the conduct of immune-based therapeutic trials and to enhance pathogenesis-related research in HIV-infected individuals.

Foster collaboration and better interactions with industry in developing and evaluating immunorestorative/immune-enhancing agents.

Define the mechanisms of immunomodulating agents and proceed with preclinical studies of the most promising agents.

Objective 4: Discover, develop, and evaluate potential agents for prevention and treatment of HIV-associated OIS and other infections modified by HIV infection.

Description: Opportunistic infections (OIs) are the most common cause of morbidity and mortality in HIV-infected individuals. Continuing to develop and evaluate therapies for preventing and treating OIs is essential for decreasing morbidity and improving survival.

Action Steps: Support basic research on OIs in order to increase fundamental knowledge and to identify new therapeutic targets and strategies and understand how pathogens contribute to morbidity. Determine the high resolution molecular structures for OI proteins and apply these structures to the rational design of drugs as part of the targeted drug development program and determine generalizable and effective approaches for the use of macromolecular structure in designing drugs to combat OIs

associated with AIDS.

Support discovery and preclinical programs to develop therapies especially targeting cryptosporidia, microsporidia, JC virus, HPV, and azole-resistant fungal organisms, with emphasis on bioavailable agents with favorable pharmacokinetics. Develop *in vitro* culture systems for OIs such as *Pneumocystis carinii* (PCP).

Further conduct clinical trials for the prophylaxis and treatment of HIV-associated OIs in HIV-infected individuals. Important OIs include *Mycobacterium tuberculosis* infection (TB), *Mycobacterium avium* complex, cytomegalovirus infection, cryptosporidiosis, microsporidiosis, cryptococcal disease, azole-resistant fungal infection, toxoplasmosis, PCP, acyclovir-resistant herpes infections, progressive multifocal leukoencephalopathy (PML), bacterial infections, and other infections whose course is affected by HIV. Evaluate immune-based therapies as adjuncts for treating OIs.

Determine the optimal strategies and combinations of agents to prevent and treat multiple OIs (by simultaneous prophylaxis of multiple opportunistic pathogens) and determine their effects in combination with antiretroviral agents. Strategies need to focus on the subgroups at increased risk, time of initiation, compliance, pharmacologic interactions, toxicities and adverse reactions (e.g. trimethoprim sulfamethoxazole reactions), and minimizing development of resistance; studies should include quality-of-life assessments and cost-benefit analyses.

Develop and utilize animal models for preclinical efficacy, pharmacokinetics, and safety testing of potential agents for OIs, including mutagenicity and teratogenicity.

Develop clinically useful assays for the rapid diagnosis of disease, treatment response, and sensitivity testing of OIs, especially TB, MAI, enterics, and infections produced by CMV, fungi, Toxoplasma, and JC virus, including use of specimens in existing repositories.

Determine the role and capability of preexisting immunity (both induced and natural) to control OIs and the ability of HIV-infected individuals to respond to vaccination throughout the course of infection and disease; assess possible interaction of vaccination and HIV replication.

Explore the bidirectional interactions between OIs and HIV infection including possible impact of opportunistic pathogens on the clinical expression and acceleration of HIV disease and vice

versa.

Support clinical trials to evaluate the safety and pharmacokinetics of existing and experimental agents for use in preventing and treating OIs in HIV-infected infants, children, and pregnant women.

Objective 5: Develop, evaluate, and implement strategies for interrupting vertical transmission of HIV from mother to child and extend out understanding of perinatal transmission and the pathogenesis of early infection (treatment of children will be addressed in other objectives).

Description: Vertical transmission of HIV from mother to child is the predominant mode of transmission for pediatric HIV infection. The identification, development, and testing of interventions should be based on the pathogenesis of transmission.

Action Steps: Support the rapid translation of basic research observations to strategies for the interruption of vertical transmission; apply the results of clinical trials to the investigation of pathogenesis and to clinical practice.

Support national and international collaborative studies to retrospectively and prospectively evaluate potential obstetric factors associated with vertical transmission including non-protocol use of antiretroviral agents.

Develop and evaluate strategies for interrupting the vertical transmission of HIV from pregnant women to their offspring that are simpler and less costly than the current AZT regimen and derive information on pathogenesis of transmission from the study of these strategies. Such strategies include antiviral agents, anti-HIV immunoglobulin, monclonal antibodies, vitamin supplementation (e.g. vitamin A), HIV vaccines, adjuvants, virucides, and other intrapartum interventions alone and in combination.

Evaluate the safety, toxicity, pharmacokinetics, and antiretroviral activity of anti-HIV agents in pregnant women and newborns; explore the use of highly active agents that may develop resistance rapidly and could be used in this setting.

Assess the potential efficacy and feasibility of obstetric interventions to prevent vertical transmissions, such as cesarean deliveries and other aspects of intrapartum care.

Develop and improve sensitive and specific diagnostic parameters

that are accessible and cost-effective to permit early differentiation of HIV infection status in children born to HIV-infected mothers.

Investigate the role of the placenta in transmission of anti-HIV drugs from mother to fetus.

Expand the obstetrical and pediatric infrastructure for the conduct of perinatal trials through collaborative efforts, particularly in the international setting.

Support the long-term follow-up of women and children who participate in perinatal trials to evaluate potential distant effects of antiretroviral agents and/or biologics.

Evaluate the risk of vertical transmission of drug-resistant virus.

Evaluate incorporation of ACTG 076 AZT regimen into clinical practice in the United States.

Evaluate therapeutic strategies for treating infants during acquisition of HIV to determine whether disease progression can be significantly altered.

Objective 6: Discover, develop, and evaluate improved strategies for the treatment and prevention of HIV-associated malignancies and extend our understanding of the risk factors for and pathogenesis of such malignancies.

Description: HIV-associated malignancies have a significant impact on morbidity and mortality, and some are expected to become increasingly common as survival with sever immune dysfunction is prolonged and as the demographics of HIV infection change. The development of methods to identify persons at high risk for subsequent malignancy, and the identification, development, and clinical testing of new therapeutic strategies for these malignancies are essential.

Action Steps: Support basic research on HIV-associated malignancies to increase fundamental knowledge of the etiology, pathogenesis, and biology of these neoplasms; develop preclinical models for testing potential therapeutic strategies.

Identify novel mechanisms and targets (e.g. cytokines, angiogenesis, viral or hormonal co-factors) for treatment and prevention of HIV-associated tumors, including Kaposi's sarcoma (KS), non-Hodgkin's lymphoma, HPV-associated malignancies, and

others, and develop new therapeutic strategies on the basis of these findings.

Use structural biologic and biochemical information to rationally design drugs to inhibit specific pathogenic factors of HIV-associated malignancies.

Develop *in vivo* models (SCID/nude mouse) for pathogenesis and drug sensitivity testing.

Develop *in vitro* models of KS as well as assays for angiogenesis inhibitors.

Encourage the develop and coordinate the conduct of clinical trials that concurrently evaluate antiretroviral and anti-OI therapeutic strategies directed against the malignancy in order to assess the effects of such treatment on the malignancy as well as on the underlying HIV infection, immune function, and clinical course.

Continue and expand screening, discovery and development of novel therapeutic agents with activity against HIV-associated malignancies (e.g. agents with better CNS penetration, agents with better safety profiles).

Develop trials to optimize existing therapies for malignancies in HIV-infected patients, including therapeutic adjuncts such as hematopoietic colony-stimulating factors and supportive care; develop and validate quality-of-life assessments.

Encourage collaborative studies to develop mechanisms for early identification of patients at high risk for malignancy and to develop and assess interventional strategies to reduce or prevent the development of malignancies.

Improve diagnostic methods for early diagnosis of malignancies and for early detection of recurrent cancer.

Improve collaboration between various adult and pediatric cooperative groups conducting clinical trials of HIV-associated malignancies and ICDs and industry to accelerate trials completion and approval of active agents.

Foster prompt referral of patients (co-registration) from antiretroviral trials to trials for AIDS-related malignancies.

Objective 7: Develop strategies for assessing,preventing, and treating central and peripheral nervous system dysfunction in the

course of HIV infection.

Description: Nervous system impairment, including AIDS-related cognitive/motor dysfunction (formerly AIDS dementia complex), and peripheral nerve/spinal cord dysfunction are serious sequelae of HIV disease.

Action Steps: Develop novel strategies and agents that are active against putative pathways of HIV-induced CNS dysfunction, e.g inhibitors of quinolinic acid, excitatory neurotransmitters, gp160/120, and other potential neurotoxins.

Implement studies related to the delineation of mechanisms responsible for impaired neurocognitive development in children born to HIV-infected mothers, and develop strategies directed at the prevention and treatment of this complication of HIV infection; utilize insights from the impaired state to better understand the course of normal neurocognitive development.

Implement clinical trials addressing nervous system complications of HIV infection and incorporate neurologic and neuropsychological assessments into other HIV-related clinical trials.

Develop therapeutic agents and/or delivery systems that are capable of crossing the blood-brain barrier and develop carriers that capitalize on different mechanisms to deliver drug to the CNS and are active against HIV infection; assess the safety of these different preparations; develop an understanding of physical and physiological mechanisms involved in penetration of the blood-brain barrier, and possibly develop agents that could conceivably block HIV entry into the CNS.

Better delineate etiologies of peripheral neuropathy in HIV infection, and develop strategies to prevent and treat this complication.

Develop and utilize *in vitro* and animal models of CNS impairment and AIDS-related cognitive/motor dysfunction to further identify agents that can reverse HIV neuropathogenesis.

Implement assessments and approaches for the diagnosis of HIV-related dementia in clinical studies; improve implementation of standardized adult, adolescent, and pediatric neuropsychologic and neurologic assessment batteries in clinical studies and evaluate treatment-induced changes in neurocognitive impairment in a linguistically and culturally sensitive context.

Develop alternative methods for detecting and assessing response to treatment of central and peripheral nervous system dysfunction including brain structural, spectroscopic, and functional imaging (for dementia); develop quantitative summary testing and examination of cutaneous nerve fibers in neuropathy.

Objective 8: Develop and evaluate therapies for the treatment and prevention of serious HIV-associated complications, especially

wasting syndrome and growth failure, as well as other disorders including hematologic, dermatologic, renal, metabolic, pulmonary, and oral manifestations.

Description: Important clinical sequelae of HIV infection include wasting syndrome, growth failure, metabolic disorders, dermatologic disorders, ITP, nephropathy, oral diseases, and other symptoms and serious complications. Drugs and strategies that can treat these sequelae are needed to ameliorate these conditions.

Action Steps: Develop and evaluate therapeutic strategies for preventing and ameliorating the various sequelae of HIV infection (listed above in the Description) and increasing understanding of their pathogenesis.

Develop and validate quality-of-life parameters for adults and children for the various sequelae of HIV infection (listed above in the Description).

Develop and evaluate therapeutic strategies for alleviating the various symptoms of unclear etiology in HIV-infected persons (listed above in the Description) and improving the quality of life.

FY 95: $462,929,000
FY 96: $472,944,000
FY 97: $470,042,000

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Unmet Needs: The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $75,363,000 over the FY 1997 figure.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To conduct and support basic, preclinical, and clinical research to develop a safe and effective preventive HIV vaccine.

Objective 1: Increase scientific knowledge of host defense mechanisms leading to protection against HIV infection and disease.

Description: More basic knowledge is needed to define protective immune responses to HIV in order to facilitate the development of vaccines and other immunologic strategies to prevent and control HIV infection.

Action Steps: Develop animal models that are practical and as much as possible are representative of the spectrum of HIV infections and AIDS; models should be amenable to use in evaluating protection by vaccines and, where this can be demonstrated, determining the correlates of protective immunity.

Determine the mechanisms of immunologically mediated control of infection with HIV and other related retroviruses, including the role of specific and nonspecific immunity in inhibiting viral replication.

Additional basic knowledge is needed to determine:

- factors, including persistence of antigens, that favor establishment of memory and development of long-term protective immunity;
- the heterogeneity of specific responses to an immunogen within distinct compartments of the immune system;
- factors that promote development of particular effector cell types;
- mechanisms resulting from exposure to HIV that interfere with induction or propagation of vaccine-induced effector responses;
- mechanisms of virus neutralization.

Study acutely infected individuals, exposed/uninfected humans (and other primates), and rapid/nonprogressors to determine viral and host factors that impact amounts of circulating virus and disease course; ensure that plasma, PBMC, biopsy, autopsy, and

other key patient and animal samples, including CNS samples, are accessible to qualified laboratories.

Define and characterize viral B cell and T cell epitopes that induce protective immunity; understand their structure and antigenicity and determine whether and how their immunogenicity can be exploited in vaccine development; and define epitopes in which substitutions cannot be tolerated by the virus.

Determine whether infection with one strain of HIV or related retroviruses confers protection against subsequent infection with a second strain; determine the protective mechanism and timing.

Understand how and why HIV and related lentiviruses evade or escape from humoral and cellular arms of the immune response.

Explore strategies to elucidate the obligate mechanisms for protective immunity against HIV, including amplification of selected responses by passive transfer of Ab or immune cells and subtraction by deletion of selected components of the immune system.

Study chronic infection with attenuated viruses, such as SIV variants shown to induce strong protection against virulent SIV strains in macaques, to understand what properties of the virus and the immune system are responsible for lack of disease induction and protection from challenge with wild-type virus.

Explore the molecular epidemiology and serology of HIV-1 populations relevant to vaccine trials and collect clinical material from these populations for scientific analysis. Acquire epidemiological information to assist in interpretation of these analyses.

Develop quantitative measures of HIV concentration in bodily fluids to determine whether there is a relationship between HIV concentration and transmission and to determine the effect of concurrent STDs on HIV shedding.

Objective 2: Apply findings from basic, epidemiologic, and clinical research to the design and evaluation of vaccine strategies in laboratory studies and animal models, and foster collaboration with industry in the research and development of candidate vaccines.

Description: The identification of viral antigens and vaccine delivery methods that elicit long-lasting protective immune responses against a broad range of HIV isolates will facilitate

development of effective vaccines.

Action Steps: Support the design and development of potential vaccines, including vaccines composed of:

- whole-killed HIV and genetically engineered, noninfectious HIV mutants that lack the viral RNA genome or have a defect in a critical gene necessary for replication but contain an array of HIV genes for expression of antigenic proteins;
- live, recombinant viral and bacterial vectors engineered to express one or more HIV proteins;
- naturally occurring and genetically engineered, live-attenuated strains of HIV;
- synthetic peptide candidates capable of inducing and boosting both cellular and humoral immunity;
- DNA coding for viral proteins;
- agents that stimulate mucosal immune responses;
- a combination of the above agents and preparations;
- other novel agents and preparations.

Evaluate the efficacy of vaccine strategies in animal models of HIV and related lentiviruses. To accomplish this:

- test vaccine strategies in animal models that most closely mimic the HIV infection in humans;
- determine the effect of vaccine formulation and regimen as well as the nature, timing, and route of vaccine challenge on the characteristics and effectiveness of the vaccine-induced immune response;
- define the impact of different vaccine approaches on kinetics of immune responses, kinetics and localization of viral replication, disease progression, and biologic characteristics of breakthrough virus including transmissibility;
- conduct long-term follow-up of vaccinated animals that become chronically infected to determine the impact of vaccination on disease progression;

- develop assays to distinguish between infection and serological responses due to immunization.

Support design and development of methods to improve or modulate immune responses (qualitatively or quantitatively), including:

- novel adjuvants and presentation methods;
- vaccines incorporating cytokines or other biologically active molecules;
- establishment of physical or biological reservoirs for long-term antigen presentation;
- other novel strategies.

Encourage development of candidate vaccines of suitable antigenic types and possessing stability and route of administration

characteristics appropriate for international as well as domestic use.

Characterize and evaluate the potential negative side effects of candidate vaccines, including production antibodies enhancing neurotoxicity and oncogenicity.

Develop better *in vitro* methodologies to measure immune responses to primary viral isolates.

Develop infrastructure, and address scientific, legal, and regulatory issues to foster and encourage participation by, and collaboration with, industry and other agencies in the research, development, production, and clinical testing of candidate vaccines.

Objective 3: Select candidate vaccines or concepts suitable for Phase I and Phase II trials and conduct these trials.

Description: Suitable candidate vaccines need to be selected and evaluated in Phase I and Phase II trials to determine safety and immunogenicity.

Action Steps: Support the conduct of Phase I and Phase II coordinated clinical trial that will determine long-term and short-term safety and compare immunologic responses to preventive vaccine candidates; include a broad range of humoral, cell-mediated, and mucosal immune parameters;

Develop a mechanism to evaluate the suitability of vaccine candidates for entry into Phase I and Phase II trials; evaluation criteria should include originality and intrinsic value of the concept and animal model data.

Develop strategies at the local and national levels to reduce social and economic risk to volunteers in Phase I and Phase II trials to facilitate broad participation.

Design and conduct Phase II trials using promising HIV vaccines that are also genetically or immunologically related to HIV isolates circulating in the proposed trial population and of an appropriate size to facilitate decisions regarding efficacy trials. Analyze immune responses in vaccines and appropriate controls. Isolate and characterize virus and follow clinical course and immune responses of vaccines who become HIV-infected.

Study viral isolates from participants in HIV vaccine trials and selected controls to explore the possible effects of vaccination on the characteristics of transmitted viruses.

Conduct behavioral research on trial participants to establish whether their risk behavior has been influenced by participation in a vaccine trial, with emphasis on individuals who become infected while participating.

Closely coordinate the evaluation of research findings on prophylactic AIDS vaccines with preclinical research and immunotherapeutic interventions.

Objective 4: Identify mechanisms of protective immunity to HIV in newborns and infants and support the development of safe and effective immunologic strategies for preventing or controlling HIV infection in this population.

Description: Distinct approaches and infrastructure are needed to achieve protection of newborns and infants because of the unique nature of their immune responses and modes of exposure to HIV.

Action Steps: Determine what viral, immunologic, and non-immunologic host factors influence transmission of HIV-1 from mother to infant;

- Compare virus isolates that are and are not transmitted from mother to infant;
- Seek maternal and infant immune responses that might prevent transmission to infants.

Develop and maintain domestic and international infrastructure necessary to enroll mothers and infants in prospective long-term follow-up vaccine trials and other interventions.

Determine the safety and immunogenicity of various HIV vaccines and adjuvants in relevant animal models of maternal-fetal and maternal-infant transmission to evaluate safety, immunogenicity, and efficacy of candidate vaccines.

Select and evaluate antibody and/or cellular preparations in passive or passive/active HIV prevention studies.

Establish criteria for advancement of candidates in Phase I, Phase II, and Phase III clinical trials in children.

Conduct Phase I, Phase II, and Phase III clinical trials in children for the most promising candidates that meet established criteria.

Objective 5: Identify appropriate domestic and international population and develop infrastructure and collaborations with government, communities, and industry necessary for ensuring adequate performance of Phase III efficacy trials.

Description: Preparation for HIV vaccine efficacy trials requires development of an infrastructure and a series of studies and planning activities to ensure their feasibility.

Action Steps: Develop domestic and international sites with access to populations at high risk for acquiring HIV infection, where vaccine or other prevention research activities may be feasible.

Establish linkages with communities or community organizations where efficacy trials might be conducted to optimize education, recruitment, and follow-up activities and to help address community concerns related to AIDS vaccine efficacy trials.

For international trials, work closely with national (host) governmental and regulatory authorities, collaborating institutions, vaccine manufacturer(s), and the World Health Organization to plan and conduct vaccine efficacy trials adhering to the highest ethical and scientific standards.

Carry out appropriate epidemiologic studies that determine the risk profiles and infection rates of various populations in the United States and worldwide in order to identify those groups most likely to be the participants in vaccine trials.

Maintain the necessary laboratory infrastructure at designated sites for conducting domestic and international vaccine efficacy trials.

Acquire and analyze HIV isolates from recent seroconverters representative of potential efficacy trial populations so that genetic and antigenic information about virus circulating in the population can be obtained.

Evaluate other biomedical and behavioral interventions that could prove of benefit in decreasing the incidence of HIV infection in the populations identified for future vaccine efficacy trials and assess their potential impact on the evaluation of vaccine efficacy.

Conduct behavioral research in populations at high risk for HIV infection to determine, for example, appropriate risk-reduction interventions and to estimate risk behavior and recruitment, adherence, and retention strategies pertinent to the design and execution of a successful efficacy trial, especially for populations that have been historically underrepresented in clinical trials.

Determine possible adverse social, economic, or legal consequences of participation in clinical trials, and develop strategies for mitigating potential harm.

Determine optimal methods of achieving informed consent for vaccine efficacy trials.

Prepare for adequate long-term follow-up of individuals participating in vaccine clinical trials where it will be necessary to determine the longevity of immune response, the correlates of immune protection, long-term safety, the impact of participation on risk-taking behavior, and the possible positive or negative effects of vaccine immunization against disease progression and HIV transmission.

Encourage linkage between vaccine preparedness studies in high-risk populations and other research activities including research on TB and STDs; and integrate research on vaccines against opportunistic infections as appropriate.

Objective 6: Select suitable vaccine candidates and support efficacy trials when appropriate criteria are met.

Description: Conduct HIV vaccine efficacy trials of the most promising candidate vaccines in well-characterized, high-risk

populations to identify effective vaccines for the control of HIV infection.

Action Steps: Establish criteria with concurrence of an advisory group that has the requisite scientific, public health, government and community expertise.

Conduct large-scale efficacy trials of preventive vaccine candidates that have proven promising, safe, and immunogenic in Phase II trials and that meet appropriate criteria;

- Evaluate HIV vaccine candidate efficacy against infection and disease;
- Evaluate additional virologic, immunologic, and behavioral outcomes, particularly correlates of protective immunity.
- Ensure that trials are conducted with the highest regard for social and ethical standards.

FY 95: $100,399,000
FY 96: $109,533,000
FY 97: $116,132,000

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Unmet Needs: The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $38,639,000 over the FY 1997 figure.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To conduct and support behavioral and social science research to further understanding of the determinants and processes that influence behaviors associated with HIV transmission and to develop and improve HIV prevention intervention strategies.

Objective 1: Support research to develop and evaluate social and behavioral interventions at the societal, community, organizational, and individual levels to reduce HIV transmission by reducing HIV-related risk behaviors and increasing protective behaviors. Multi-site and cross-national studies are encouraged.

Description: Studies have demonstrated that HIV-related risk behaviors can be measured and modified. In response to the evolving epidemic, an expanded HIV prevention research agenda is called for on what works, for whom, where, for how long, and at what cost.

Action Steps: Develop and evaluate the effectiveness and cost-effectiveness of demographically and culturally appropriate behavioral and social interventions in different domestic and international settings and populations to reduce high-risk HIV-related behaviors and HIV transmission (e.g. through safer sexual practices, increased use of condoms and other barrier methods, use of sterile injection equipment, and reduction of high-risk drug-related behaviors).

Support research on a range of HIV prevention strategies in a variety of settings for both emerging populations and groups that continue to be at high risk for HIV.

Support research to increase the effectiveness and cost-effectiveness of drug abuse, mental health, and alcoholism treatment, including the development of new pharmacotherapies, to reduce HIV-related risk behavior in different settings and populations.

Support research (including multi-site and cross national studies) on comprehensive interventions that integrate various HIV and STD prevention and family planning approaches.

Support research to improve the access to, delivery of, evaluation, and cost-effectiveness of services that reduce HIV risk behaviors and transmission.

Design and test interventions to increase recruitment, retention, and adherence to protocols for HIV prevention research, including prophylactic vaccines.

Support research to improve the transfer of effective interventions to and from community planning processes.

Objective 2: Support basic research to strengthen the understanding of determinants and processes that influence HIV-related risk behaviors and the consequences of HIV disease.

Description: Understanding the basic factors influencing behavior and behavior change at the societal, community, organizational, and individual levels is necessary for the development of interventions to prevent the transmission of HIV and to ameliorate its adverse consequences. Research is needed to define the behavioral, psychological, cognitive, and social consequences of HIV infection, disease progression, and treatment.

Action Steps: Develop models of behavior and behavior change that integrate biological, psychological , and social perspectives to explain and predict the acquisition, change, and maintenance of HIV-related behaviors among individuals and groups in various settings.

Study the social, structural, and cultural factors such as class, ethnicity, sexual identification, age, and gender that influence HIS-related behavior, affect access and delivery of care, and determine intervention strategies.

Study the development and maintenance of HIV-related risk and preventive behaviors in specific social contexts such as the sexual dyad, peer groups, social and drug-using networks, families, and communities.

Conduct research on decision-making processes, which may include disclosure of one's HIV-status, choice of treatment options, and adoption of protective behaviors.

Support research to understand the processes of how communities become involved in HIV intervention research.

Identify the behavioral, psychological, cognitive, and social consequences of HIV disease for HIV-seropositive individuals, their support systems (e.g. partners, family members, and other care givers), and their communities.

Support studies in animal models in behavior and behavior change relevant to HIV infection and prevention.

Conduct research that identifies the social and behavioral factors affecting recruitment, retention, and adherence in clinical trials.

Conduct research on the barriers to preventive actions based on lack of trust and misinterpretations of meaning of information related to HIV.

Objective 3: Support research for the discovery, development, and evaluation of strategies for preventing or minimizing the negative physical, psychological, cognitive, and social consequences of HIV, including stigmatization of persons with or at-risk for HIV infection. Support research strategies for promoting effective health care utilization among persons with HIV infection.

Description: Enhancement of the quality of life of seropositive individuals and facilitation of HIV treatment require further research on interventions to affect the physical, behavioral, psychological, cognitive, and social consequences of HIV infection, disease progression, and treatment. Research is also needed to improve delivery of care to diverse population groups.

Action Steps: Develop and evaluate interventions for promoting quality of life and to delay or prevent physical, behavioral, psychological, cognitive, and social consequences.

Promote research to identify and remove barriers to effective health care utilization among persons with or at-risk of HIV infection, including access, engagement, follow-up, and adherence to health and social services across the care continuum (e.g. testing and counseling, health care-seeking behavior, adherence, case management, and home/hospice care). This strategy may entail developing and testing innovative models of treatment delivery for HIV disease at all illness stages.

Develop and evaluate interventions for promoting increased recruitment, adherence, and retention, especially in underrepresented populations, in HIV treatment and clinical trials.

Test models of care-giving for people living with HIV disease, their significant others, extended family members, and care providers.

Develop and evaluate interventions for preventing social stigmatization of persons with or at-risk of HIV infection and AIDS in different settings (e.g. workplaces, schools, health care facilities, and prisons).

Objective 4: Support research to advance innovative quantitative and qualitative methodologies to enhance HIV behavioral and social science research.

Description: Behavioral and social science methods have greatly advanced our understanding of HIV transmission and health maintenance. Further refinement of established methods and rapid development of emerging technologies are essential to continued improvement of our knowledge of HIV-related behaviors; our understanding of linkages between HIV-related risk behaviors, transmission, and disease progression; and the evaluation of interventions.

Action Steps: Develop improved qualitative and quantitative methodologies for studying behavioral and social factors associated with HIV, including improved methods for validating self-report data, improved measurement tools for surveys, and the measurement of change over time.

Develop improved sampling strategies for sub-populations and culturally and linguistically sensitive and appropriate research instruments.

Develop improved methods and techniques for dealing with subject attrition and missing data.

Encourage secondary data analysis by developing techniques to protect confidentiality and by using of meta-analysis.

Develop and refine techniques for measuring social networks associated with HIV.

Develop and refine research techniques for measuring responses by organizations to HIV and for characterizing organizations working in the HIV field.

Encourage studies that will support multi-site studies and cross-national comparisons.

Develop and refine mathematical models for linking behavior change interventions with reduction in HIV transmission.

FY 95: $170,984,000

FY 96: $174,077,000
FY 97: $180,238,000

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Unmet Needs: The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $25,655,000 over the FY 1997 figure.

Agency: Department of Health and Human Services, National Institutes of Health

Goal: To provide appropriate training and infrastructure for the conduct of HIV-related biomedical and behavioral research domestically and internationally.

Objective 1: Provide both domestic and international training in biomedical and behavioral research on HIV.

Description: Meeting the needs of research on HIV/AIDS requires recruiting and training basic, clinical, and behavioral scientists in the United States and abroad in the many disciplines necessary to carry out this diverse scientific agenda.

Action Steps: Increase pre-doctoral and post-doctoral training, as well as advanced research training, in a range of AIDS-related disciplines to a level comparable (about 3 percent of the budget) to that of other training programs within NIH.

Sponsor an annual AIDS Fellows Meeting to promote collaboration and information dissemination.

Increase training of scientists and clinical investigators in basic AIDS research to better link basic and clinical pathogenesis research.

Stimulate pre-doctoral and post-doctoral training in prevention, behavior change, and adherence and compliance to treatment.

Promote training of biomedical and behavioral scientists in the use of high-performance computing systems for HIV-related research.

Expand training and research capacity to deal with the epidemic of tuberculosis (TB), including multiple drug resistance associated with HIV infection.

Increase participation in the Fogarty International Center (FIC)-sponsored international training and research programs and expand these programs by recruiting trainees from additional countries in Asia and Latin America, with the long-term goal of providing AIDS-related training for leading health scientists from all developing countries.

Develop new grant mechanisms to link U.S. AIDS research scientists and institutions with leading AIDS research

scientists and institutions in foreign countries.

Expand both pre-doctoral and post-doctoral training in structural biology.

Expand the NIH AIDS Loan Repayment Program to bring scientists and physicians to the NIH to expand the cadre of trained intramural researchers.

Expand both pre- and post-doctoral domestic and international AIDS-related training in epidemiology, biostatistics, and behavioral methodologies.

Establish and expand appropriate career training programs for laboratory investigators, clinical investigators, and translational scientists (i.e. making the transition from bench to patient).

Enhance training of investigators in applied immunobiology.

Support training of basic investigators, clinical investigators, and translational investigators for OI research.

Support training of basic investigators, clinical investigators, and translational scientists for research on malignancies in HIV-infected patients.

Collaborate with other PHS agencies in the development of training regarding HIV prevention, treatment, research, and education for health care providers, AIDS service providers, and health educators.

Objective 2: Establish appropriate infrastructure for the conduct of HIV research domestically and internationally.

Description: The conduct of HIV research in the United States and abroad requires establishment of infrastructure to carry out this research program, including facilities and instrumentation, computers, data communications, laboratories, and animal colonies.

Action Steps: Provide additional facilities to study animal models of pediatric AIDS.

Foster animal models to study HIV-related malignancies.

Continue the Research Facilities Infrastructure Program (RFI) and

General Clinical Research Centers (GCRC) Program.

Expand the use of the National Research and Education Network (NREN) for national and international collaboration and data communications.

Provide for expansion of breeding facilities to ensure the adequate supply of species of emerging importance, e.g. *M. nemestrina.*

Provide NCRR animal model support tied to needs of basic research grants.

Provide for the long-term support of advanced in-country research and research infrastructure in those developing countries participating in efficacy trials of candidate HIV vaccines and other priority intervention research.

Develop and support animal models predictive of human behavior, specifically, models of non-human primate behavior of impaired impulse control and risk-taking.

Provide additional laboratory and biocontainment facilities for primate research.

Increase support for the Internet connections program at health sciences centers and hospitals for research and patient care.

Establish and support repositories of samples obtained from individuals with HIV infection for current and future studies.

Increase support for screening the development of HIV macaque monkey models.

Develop and support Regional Primate Research Center (RPRC) expertise in molecular immunology, peptide biochemistry, and pharmacology.

Provide for the establishment of specific pathogen-free (SPF) non-human primate programs at all the RPRCs.

Provide further support for the development of SPF macaque colonies.

FY 95: $46,483,000
FY 96: $44,643,000
FY 97: $44,335,000

Populations Served: All populations.

Constituency Involvement: Researchers, clinicians, community and patient representatives, and NIH-affiliated advisory councils and committees.

Unmet Needs: The NIH FY 1996 Plan and Budget Estimate for Scientific Opportunities in HIV-Related Research identified areas for further productive research in this area in the amount of $14,368,000 over the FY 1997 figure.

Agency: Department of Justice

Goal: To estimate the prevalence of HIV/AIDS among the corrections and parole population and to monitor the HIV/AIDS-related policies of Federal, State, and local correctional agencies.

Objective: Data collection and dissemination of periodic reports.

Action Steps: Conduct surveys of federal, state and local prisons and inmates and publish results in periodic reports.

Descriptions: When published, the 1995 Survey on Probation, the 1996 Survey of Inmates in Local Jails, and the 1997 Survey of State and Local Federal Inmates in Adult Correctional Facilities will contain estimates of HIV prevalence among probationers and inmates, and characteristics of this HIV positive population.

Publication of reports describing findings of multi-year project, "HIV Education in Lockups and Booking Facilities."

1994 Survey of HIV/AIDS in Correctional Facilities.

Publication of 1996 report "HIV/AIDS and STDs in Juvenile Facilities."

Census of prison, survey of jail and prison inmates and probationers, and study examining research on prevention programs directed towards at persons whose behavior makes them vulnerable to HIV infection.

FY 95: Part of overall operating budget.
FY 96: Part of overall operating budget.
FY 97: Part of overall operating budget.

Populations Served: Department of Justice, corrections administrators, and public.

Constituency Involvement: None.

Unmet Need: Funding for research into requirements for effective management of HIV positive inmates.

Funding to conduct surveys of individual facilities and increase surveys of the juvenile system, and to conduct additional work in the areas of prevention and education.

Agency: Department of Veterans Affairs

Goal: To utilize the unique resource of the VA-served patient population to further biomedical, health services, and rehabilitation research on HIV and AIDS.

Objective 1: Support AIDS-related research as a high priority area within the VA-served patient population utilizing the unique resources.

Action Steps: Fund research with high technical and scientific merit.

Continue to fund AIDS-related research through existing funding mechanisms, i.e., investigator-initiated studies, cooperative studies, and research centers.

Collaborate with other federal departments and agencies in initiating and conducting AIDS relevant research (including joint funding of projects), thereby making the unique resources of VA available to collaborating investigators.

Provide applicants for research support with feedback on the technical and scientific quality of their proposals.

Objective 2: Develop and maintain AIDS Research Centers to stimulate and emphasize importance of HIV/AIDS research in VA's unique population.

Action Steps: Establish AIDS Research Centers based on competitive proposal basis.

Objective 3: Encourage collaboration with other Federal departments and agencies in initiating and conducting AIDS-related research.

Action Steps: Facilitate investigator requested funding by NIH, other Federal agencies.

Support participation in community trials on individual investigator and medical center basis.

Objective 4: Disseminate research findings.

Action Steps: Publish and present findings of research in peer reviewed journals, and at national and international conferences.

Description: Research activities.

FY 95: $ 5,400,000 *
FY 96: $ 5,700,000 *
FY 97: $ 5,700,000 *

(* Estimated expenditures for HIV/AIDS research are part of the general Medical and Prosthetics Research budgets. FY 1996 and FY 1007 estimates are based on the resource levels contained in the President's budget.)

Populations Served: Veteran patients, general public, researchers.

Constituency Involvement: Veteran patients, scientific community, general public at large.

Unmet Need: Increased funding would enhance ability to involve VA's unique population in research and thereby increasing patients' access to research and the research knowledge base.

Agency: Department of Treasury

Goal: Through tax code policies, provide incentives for privately-sponsored research, including HIV-related research.

Objective: Encourage private sector investment in medical research, including HIV-related research.

Action Steps: Support the revenue neutral extension of the Research and Experimentation Tax Credit and the Orphan Drug Tax Credit.

Descriptions: Research and Experimentation (R&E) Tax Credit and Orphan Drug Tax Credit.

FY 95: Not applicable.
FY 96: Not applicable.
FY 97: Not applicable.

Populations Served: Private sector entities supporting research.

Constituency Involvement: The National AIDS Drug Development Task Force, comprised of industry and government representatives and patient advocates, supported these policies.

Unmet Need: None.